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lication	e diseas	thritis,	nematos	nd/or as		; (e.g., a	oosting	ne	essing a	ne	I highly	s includ		lers. Ar	eferred	nn (e.g.,	describ	ious	rred	neoplast	mia,	s descri			pa	neoplasr	for,	lympho	1180
erred inc	immune	atoid an	us eryth	erosis ar	low),	ciencies	low), be	d immu	d suppr	d immu	lditiona	lication	n and	y disord	ghly pre	infection	sease as	"Infect	Preferred	nclude 1	., leuke	und/or a		erative	Preferre	nclude r	such as	kemia,	hreact
Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response. Additional highly	preferred indications include	inflammation and	inflammatory disorders. An	additional highly preferred	indication is infection (e.g., an	infectious disease as described	below under "Infectious	Disease").	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	and progtate breast line
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ability		ntibodie	nists of	ate	ctors an	f genes		nctions.		he	nt that	·ly		ity of	ention	pu	of the	ys	ıl., Gen	and	ymol	enthorn	sci USA		Med	; De	em Cell	(1999)	loui.
ess the	s of the	uding aı	antago	o regula	otion fa	ssion o		atory fu	ys for	rough tl	eleme	routine	t NFAT	nt activ	the inv	odies a	gonists	ıde assa	rger et	Cullen	s in Enz	992); H	Acad §	1988);	JExp	(1995)	Bioch	:1-1236	r I Imm
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modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to regulate	NFAT transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Aramburu et al., J Exp Med	182(3):801-810 (1995); De	Boer et al., Int J Biochem Cell	Biol 31(10):1221-1236 (1999);	Fraser et al Fur I Immunol
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cells).																													
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				Yeseen et al., J Biol Chem	stomach, brain, liver and
				268(19) 14285-14293 (1993)	urinary cancer Other preferred
-				the contents of each of which	indications include benich
				the contents of each of which	mulcanons include beingn
-				are herein incorporated by	dysproliferative disorders and
				reference in its entirety. NK	pre-neoplastic conditions, such
				cells that may be used	as, for example, hyperplasia,
				according to these assays are	metaplasia, and/or dysplasia.
				publicly available (e.g.,	Preferred indications also
				through the ATCC).	include anemia, pancytopenia,
				Exemplary human NK cells	leukopenia, thrombocytopenia,
				that may be used according to	Hodgkin's disease, acute
				these assays include the NK-	lymphocytic anemia (ALL),
-				YT cell line, which is a human	plasmacytomas, multiple
				natural killer cell line with	myeloma, Burkitt's lymphoma,
				cytolytic and cytotoxic	arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HAIFL18	537	Activation of	Kinase assay. Kinase assays,	A highly preferred
_			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment

may be used or routinely	of the invention includes a
modified to access the shility	mothod for inhibiting
indulited to assess the admity	
 of polypeptides of the	adipocyte proliteration. A
invention (including antibodies	highly preferred embodiment
and agonists or antagonists of	of the invention includes a
the invention) to promote or	method for stimulating
inhibit cell proliferation,	adipocyte differentiation. An
activation, and differentiation.	alternative highly preferred
Exemplary assays for ERK	embodiment of the invention
kinase activity that may be	includes a method for
used or routinely modified to	inhibiting adipocyte
test ERK kinase-induced	differentiation. A highly
activity of polypeptides of the	preferred embodiment of the
invention (including antibodies	invention includes a method
and agonists or antagonists of	for stimulating (e.g.,
the invention) include the	increasing) adipocyte
assays disclosed in Forrer et	activation. An alternative
al., Biol Chem 379(8-9):1101-	highly preferred embodiment
1110 (1998); Le Marchand-	of the invention includes a
Brustel Y, Exp Clin	method for inhibiting the
 Endocrinol Diabetes	activation of (e.g., decreasing)
107(2):126-132 (1999);	and/or inactivating adipocytes.
Kyriakis JM, Biochem Soc	Highly preferred indications
 Symp 64:29-48 (1999); Chang	include endocrine disorders
 and Karin, Nature	(e.g., as described below under
 410(6824):37-40 (2001); and	"Endocrine Disorders").
Cobb MH, Prog Biophys Mol	Highly preferred indications
 Biol 71(3-4):479-500 (1999);	also include neoplastic
the contents of each of which	diseases (e.g., lipomas,
are herein incorporated by	liposarcomas, and/or as
reference in its entirety.	described below under

		Mouse adipocyte cells that	"Hyperproliferative
		may be used according to these	Disorders"). Preferred
	_	assays are publicly available	indications include blood
		(e.g., through the ATCC).	disorders (e.g., hypertension,
		Exemplary mouse adipocyte	congestive heart failure, blood
	-	cells that may be used	vessel blockage, heart disease,
		according to these assays	stroke, impotence and/or as
		include 3T3-L1 cells. 3T3-L1	described below under
		is an adherent mouse	"Immune Activity",
		preadipocyte cell line that is a	"Cardiovascular Disorders",
		continuous substrain of 3T3	and/or "Blood-Related
		fibroblast cells developed	Disorders"), immune disorders
		through clonal isolation and	(e.g., as described below under
		undergo a pre-adipocyte to	"Immune Activity"), neural
		adipose-like conversion under	disorders (e.g., as described
		appropriate differentiation	below under "Neural Activity
		conditions known in the art.	and Neurological Diseases"),
-			and infection (e.g., as
			described below under
			"Infectious Disease").
			A highly preferred indication
			is diabetes mellitus. An
			additional highly preferred
			indication is a complication
			associated with diabetes (e.g.,
			diabetic retinopathy, diabetic
			nephropathy, kidney disease
			(e.g., renal failure,
			nephropathy and/or other
			diseases and disorders as
			described in the "Renal

					Disorders" section below),
					diabetic neuropathy, nerve
			-		disease and nerve damage
					(e.g., due to diabetic
					neuropathy), blood vessel
					blockage, heart disease, stroke,
					impotence (e.g., due to diabetic
			-		neuropathy or blood vessel
		-			blockage), seizures, mental
					confusion, drowsiness,
					nonketotic hyperglycemic-
					hyperosmolar coma,
					cardiovascular disease (e.g.,
					heart disease, atherosclerosis,
	. —				microvascular disease,
-	_				hypertension, stroke, and other
					diseases and disorders as
					described in the
					"Cardiovascular Disorders"
					section below), dyslipidemia,
			-		endocrine disorders (as
	- 				described in the "Endocrine
					Disorders" section below),
					neuropathy, vision impairment
					(e.g., diabetic retinopathy and
			, ,,, ,		blindness), ulcers and impaired
					wound healing, infection (e.g.,
				-	infectious diseases and
	,				disorders as described in the
					 "Infectious Diseases" section
					below (particularly of the

urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	lymphoma, leukemia and	

				indications include melanoma
				prostate ling pancreatic
				prostate, fung, panerealle,
				esophageal, stomach, brain,
				liver, and urinary cancer.
				Highly preferred indications
				include lipomas and
				liposarcomas. Other preferred
				indications include benign
				dysproliferative disorders and
				pre-neoplastic conditions, such
				as, for example, hyperplasia,
				metaplasia, and/or dysplasia.
HAIFLI8	537	Production of	IFNgamma FMAT. IFNg plays	A highly preferred
		IFNgamma using a	a central role in the immune	embodiment of the invention
		T cells	system and is considered to be	includes a method for
			a proinflammatory cytokine.	stimulating the production of
			IFNg promotes TH1 and	IFNg. An alternative highly
•			inhibits TH2 differentiation;	preferred embodiment of the
			promotes IgG2a and inhibits	invention includes a method
			IgE secretion; induces	iţi
			macrophage activation; and	IFNg. Highly preferred
			increases MHC expression.	ns
			Assays for immunomodulatory	disorders (e.g., as described
			proteins produced by T cells	below under "Immune
			and NK cells that regulate a	Activity", "Blood-Related
			variety of inflammatory	Disorders", and/or
			activities and inhibit TH2	"Cardiovascular Disorders"),
			helper cell functions are well	and infection (e.g., viral
_			known in the art and may be	infections, tuberculosis,
_			used or routinely modified to	infections associated with
			assess the ability of	chronic granulomatosus

disease and malignant osteoporosis, and/or as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example lenkemia lymphoma
polypeptides of the invention (including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Gonzalez et al., J Clin	Lab Anal 8(5):225-233 (1995);	Billian et al., Ann NY Acad
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				Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
				et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
				15:749-795 (1997), and	esophageal, stomach, brain,
				Rheumatology (Oxford)	liver and urinary cancer. Other
_				38(3):214-20 (1999), the	preferred indications include
				contents of each of which are	benign dysproliferative
				herein incorporated by	disorders and pre-neoplastic
				reference in its entirety.	conditions, such as, for
	_			Human T cells that may be	example, hyperplasia,
				used according to these assays	metaplasia, and/or dysplasia.
				may be isolated using	Preferred indications include
				techniques disclosed herein or	anemia, pancytopenia,
				otherwise known in the art.	leukopenia, thrombocytopenia,
				Human T cells are primary	Hodgkin's disease, acute
-			_	human lymphocytes that	lymphocytic anemia (ALL),
				mature in the thymus and	plasmacytomas, multiple
			_	express a T Cell receptor and	myeloma, Burkitt's lymphoma,
	_			CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
				cells mediate humoral or cell-	disease, inflammatory bowel
				mediated immunity and may	disease, sepsis, neutropenia,
				be preactivated to enhance	neutrophilia, psoriasis,
				responsiveness to	suppression of immune
				immunomodulatory factors.	reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HAIFL18	537	Activation of	Assays for the activation of	A preferred embodiment of
		_	transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,

reducing) TNE clabs	production An alternative	highly preferred embodiment	of the invention includes a	method for stimulating (e.g.,	increasing) TNF alpha	production. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn's disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	•
(SRF) are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate serum response	factors and modulate the	expression of genes involved	in growth and upregulate the	function of growth-related	genes in many cell types.	Exemplary assays for	transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	
response element in	immune cells (such	as natural killer	cells).									-			-							-								_
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			-																									-	-	-

which are herein incorporated	preferred indication is sepsis.
by reference in its entirety. T	Highly preferred indications
cells that may be used	include neoplastic diseases
according to these assays are	(e.g., leukemia, lymphoma,
publicly available (e.g.,	and/or as described below
through the ATCC).	under "Hyperproliferative
Exemplary T cells that may be	Disorders"). Additionally,
used according to these assays	highly preferred indications
include the NK-YT cell line,	include neoplasms and
which is a human natural killer	cancers, such as, for example,
cell line with cytolytic and	leukemia, lymphoma,
cytotoxic activity.	melanoma, glioma (e.g.,
	malignant glioma), solid
	tumors, and prostate, breast,
	lung, colon, pancreatic,
	esophageal, stomach, brain,
	liver and urinary cancer. Other
	preferred indications include
	benign dysproliferative
	disorders and pre-neoplastic
	conditions, such as, for
	example, hyperplasia,
	metaplasia, and/or dysplasia.
	Preferred indications include
	anemia, pancytopenia,
	leukopenia, thrombocytopenia,
	Hodgkin's disease, acute
	lymphocytic anemia (ALL),
	plasmacytomas, multiple
	myeloma, Burkitt's lymphoma,
	arthritis, AIDS, granulomatous

				disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
HAJAF57	538	Regulation of apoptosis of immune cells (such as mast cells).	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues throughout the body, and their activation via immunoglobulin E -	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.

antigen, promoted by T helper	cell type 2 cytokines, is an	important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000);Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-	218 (2000); and Karsan and	Harlan, J Atheroscler Thromb	3(2): 75-80 (1996); the	contents of each of which are	herein incorporated by	reference in its entirety.	Immune cells that may be used	according to these assays are
							-				_																			

				publicly available (e.g.	
			· ·	through commercial sources).	_
				Exemplary immune cells that	
				may be used according to these	
	-			assays include mast cells such	
				as the HMC human mast cell	
				line.	
HAJ	HAJAF57	538	Activation of	Kinase assay. JNK kinase	A highly preferred
			Endothelial Cell	assays for signal transduction	embodiment of the invention
			JNK Signaling	that regulate cell proliferation,	includes a method for
			Pathway.	activation, or apoptosis are	stimulating endothelial cell
				well known in the art and may	growth. An alternative highly
			-	be used or routinely modified	preferred embodiment of the
-				to assess the ability of	invention includes a method
				polypeptides of the invention	for inhibiting endothelial cell
				(including antibodies and	growth. A highly preferred
	•			agonists or antagonists of the	embodiment of the invention
				invention) to promote or	includes a method for
				inhibit cell proliferation,	stimulating endothelial cell
				activation, and apoptosis.	proliferation. An alternative
				Exemplary assays for JNK	highly preferred embodiment
				kinase activity that may be	of the invention includes a
				used or routinely modified to	method for inhibiting
	-			test JNK kinase-induced	endothelial cell proliferation.
				activity of polypeptides of the	A highly preferred
				invention (including antibodies	embodiment of the invention
	_			and agonists or antagonists of	includes a method for
				the invention) include the	stimulating apoptosis of
				assays disclosed in Forrer et	endothelial cells. An
_				al., Biol Chem 379(8-9):1101-	alternative highly preferred
				1110 (1998); Gupta et al., Exp	embodiment of the invention

includes a method for	inhibiting apoptosis of	endothelial cells. A	highly preferred embodiment	of the invention includes a	method for stimulating	endothelial cell activation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting the activation of	and/or inactivating endothelial	cells. A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention include a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under
Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.					
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			-								-																			
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	"Hyperproliferative Disorders"), and disorders of
	(e.g., heart disease, congestive
	heart failure, hypertension, aortic stenosis.
	cardiomyopathy, valvular
	regurgitation, left ventricular
	dysfunction, atherosclerosis
	and atherosclerotic vascular
	disease, diabetic nephropathy,
	intracardiac shunt, cardiac
	hypertrophy, myocardial
	infarction, chronic
	hemodynamic overload, and/or
	as described below under
	"Cardiovascular Disorders").
	Highly preferred indications
	include cardiovascular,
	endothelial and/or angiogenic
	disorders (e.g., systemic
	disorders that affect vessels
-	such as diabetes mellitus, as
	well as diseases of the vessels
	themselves, such as of the
	arteries, capillaries, veins
	and/or lymphatics). Highly
	preferred are indications that
	stimulate angiogenesis and/or
	cardiovascularization. Highly
	preferred are indications that

			_																						
inhibit angiogenesis and/or cardiovascularization. Highly preferred indications	include antiangiogenic activity to treat solid tumors,	leukemias, and Kaposi"s	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi's sarcoma,	cavernous), glomus tumors.	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications
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also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or
				-					-						-															
		_																												

other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic
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							A																							
										-						-						_	-							

				inflammatory diseases, e.g., inflammatory bowel disease
				management.
HAJAN23	539	Stimulation of	Assays for measuring calcium	A highly preferred
		Calcium Flux in	flux are well-known in the art	indication is diabetes mellitus.
		pancreatic beta	and may be used or routinely	An additional highly preferred
		cells.	modified to assess the ability	indication is a complication
			of polypeptides of the	associated with diabetes (e.g.,
			invention (including antibodies	diabetic retinopathy, diabetic
			and agonists or antagonists of	nephropathy, kidney disease
			the invention) to mobilize	(e.g., renal failure,
			calcium. For example, the	nephropathy and/or other
			FLPR assay may be used to	diseases and disorders as
			measure influx of calcium.	described in the "Renal
			Cells normally have very low	Disorders" section below),
			concentrations of cytosolic	diabetic neuropathy, nerve
			calcium compared to much	disease and nerve damage
			higher extracellular calcium.	(e.g., due to diabetic
			Extracellular factors can cause	neuropathy), blood vessel
			an influx of calcium, leading to	blockage, heart disease, stroke,
			activation of calcium	impotence (e.g., due to diabetic
			responsive signaling pathways	neuropathy or blood vessel
			and alterations in cell	blockage), seizures, mental
			functions. Exemplary assays	confusion, drowsiness,
			that may be used or routinely	nonketotic hyperglycemic-
_			modified to measure calcium	hyperosmolar coma,
			flux by polypeptides of the	cardiovascular disease (e.g.,
			invention (including antibodies	heart disease, atherosclerosis,
			and agonists or antagonists of	microvascular disease,
			the invention) include assays	hypertension, stroke, and other

	disclosed in: Satin LS, et al.	diseases and disorders as
	Endocrinology, 136(10):4589-	described in the
-	601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
	Endocrinology, 136(7):2960-6	section below), dyslipidemia,
	(1995); Richardson SB, et al.,	endocrine disorders (as
	Biochem J, 288 (Pt 3):847-51	described in the "Endocrine
	(1992); and, Meats, JE, et al.,	Disorders" section below),
	Cell Calcium 1989 Nov-	neuropathy, vision impairment
	Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
	contents of each of which is	blindness), ulcers and impaired
	herein incorporated by	wound healing, and infection
	reference in its entirety.	(e.g., infectious diseases and
_	Pancreatic cells that may be	disorders as described in the
	used according to these assays	"Infectious Diseases" section
	are publicly available (e.g.,	below, especially of the
	through the ATCC) and/or	urinary tract and skin), carpal
	may be routinely generated.	tunnel syndrome and
	Exemplary pancreatic cells that	Dupuytren's contracture).
	may be used according to these	An additional highly preferred
	assays include HITT15 Cells.	indication is obesity and/or
	HITT15 are an adherent	complications associated with
	epithelial cell line established	obesity. Additional highly
	from Syrian hamster islet cells	preferred indications include
	transformed with SV40. These	weight loss or alternatively,
	cells express glucagon,	weight gain. Aditional
	somatostatin, and	highly preferred indications are
	glucocorticoid receptors. The	complications associated with
	cells secrete insulin, which is	insulin resistance.
	stimulated by glucose and	
	glucagon and suppressed by	
	somatostatin or	

				glucocorticoids. ATTC# CRL-	
			,	Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc.	
				Natl. Acad. Sci. USA 78:	
				4339-4343, 1981.	
	HAJBR69	540	Regulation of	Assays for the regulation of	A highly preferred
			transcription	transcription through the	indication is diabetes mellitus.
			through the PEPCK	PEPCK promoter are well-	An additional highly preferred
			promoter in	known in the art and may be	indication is a complication
			hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
				assess the ability of	diabetic retinopathy, diabetic
				polypeptides of the invention	nephropathy, kidney disease
				(including antibodies and	(e.g., renal failure,
				agonists or antagonists of the	nephropathy and/or other
				invention) to activate the	diseases and disorders as
				PEPCK promoter in a reporter	described in the "Renal
				construct and regulate liver	Disorders" section below),
			•	gluconeogenesis. Exemplary	diabetic neuropathy, nerve
		-:		assays for regulation of	disease and nerve damage
•				transcription through the	(e.g., due to diabetic
-				PEPCK promoter that may be	neuropathy), blood vessel
				used or routinely modified to	blockage, heart disease, stroke,
				test for PEPCK promoter	impotence (e.g., due to diabetic
				activity (in hepatocytes) of	neuropathy or blood vessel
				polypeptides of the invention	blockage), seizures, mental
				(including antibodies and	confusion, drowsiness,
				agonists or antagonists of the	nonketotic hyperglycemic-
				invention) include assays	hyperosmolar coma,
	-			disclosed in Berger et al., Gene	cardiovascular disease (e.g.,
				66:1-10 (1998); Cullen and	heart disease, atherosclerosis,

microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	an infectious diseases or	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.
Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Lochhead et al., Diabetes	49(6):896-903 (2000); and	Yeagley et al., J Biol Chem	275(23):17814-17820 (2000),	the contents of each of which	is herein incorporated by	reference in its entirety.	Hepatocyte cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary liver hepatoma	cells that may be used	according to these assays	include H4lle cells, which	contain a tyrosine amino	transferase that is inducible	with glucocorticoids, insulin,	or cAMP derivatives.						
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indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as	described herein. Additional highly preferred indications include glycogen storage disease (e.g., glycogenoses), hepatitis,	gallstones, cirrhosis of the liver, degenerative or necrotic liver disease, alcoholic liver diseases, fibrosis, liver regeneration, metabolic disease, dyslipidemia and	cholesterol metabolism, and hepatocarcinomas. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity".	"Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), infection	(e.g., an infectious disease and/or disorder as described below under "Infectious Disease"), endocrine disorders (e.g., as described below under

				"Endocrine Disorders"), and
				neural disorders (e.g., as
				described below under "Neural
				Activity and Neurological
				Diseases").
				Additional preferred
				indications include neoplastic
				diseases (e.g., as described
				below under
				"Hyperproliferative
				Disorders"). Preferred
				indications include neoplasms
				and cancers, such as, leukemia,
				lymphoma, prostate, breast,
				lung, colon, pancreatic,
	•			esophageal, stomach, brain,
				and urinary cancer. A highly
				preferred indication is liver
				cancer. Other preferred
				indications include benign
				dysproliferative disorders and
				pre-neoplastic conditions, such
				as, for example, hyperplasia,
000001111				metaplasia, and/or dysplasia.
HAJBK69	540	Production of GM-	GM-CSF FMAT. GM-CSF is	A highly preferred
		CSF	expressed by activated T cells,	embodiment of the invention
			macrophages, endothelial cells,	includes a method for
			and fibroblasts. GM-CSF	stimulating the production of
			regulates differentiation and	GM-CSF. An alternative
			proliferation of granulocytes-	highly preferred embodiment
			macrophage progenitors and	of the invention includes a

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	ciniances annimicional activity	linemod for innibiting the
	in neutrophils, monocytes and	production of GM-CSF.
	macrophage. Additionally,	Highly preferred indications
	GM-CSF plays an important	include inflammation and
	role in the differentiation of	inflammatory disorders. An
	dendritic cells and monocytes,	additional highly preferred
	and increases antigen	indication is infection (e.g., as
	presentation. GM-CSF is	described below under
	considered to be a	"Infectious Disease".
 -	proinflammatory cytokine.	Highly preferred indications
 -	Assays for immunomodulatory	include blood disorders (e.g.,
	proteins that promote the	neutropenia (and the
	production of GM-CSF are	prevention of neutropenia
	well known in the art and may	(e.g., in HIV infected patients),
	be used or routinely modified	and/or as described below
	to assess the ability of	under "Immune Activity",
	polypeptides of the invention	"Blood-Related Disorders",
	(including antibodies and	and/or "Cardiovascular
	agonists or antagonists of the	Disorders"). Highly preferred
	invention) to mediate	indications also include
	immunomodulation and	autoimmune diseases (e.g.,
	modulate the growth and	rheumatoid arthritis, systemic
	differentiation of leukocytes.	lupus erythematosis, multiple
	Exemplary assays that test for	sclerosis and/or as described
	immunomodulatory proteins	below) and
	evaluate the production of	immunodeficiencies (e.g., as
_	cytokines, such as GM-CSF,	described below). Additional
	and the activation of T cells.	highly preferred indications
	Such assays that may be used	include asthma. Highly
	or routinely modified to test	preferred indications include
	immunomodulatory activity of	neoplastic diseases (e.g.,

	polypeptides of the invention	leukemia (e.g., acute
	(including antibodies and	lymphoblastic leukemia, and
	agonists or antagonists of the	acute myelogenous leukemia),
	invention) include the assays	lymphoma (e.g., non-
	disclosed in Miraglia et al., J	Hodgkin"s lymphoma and
	Biomolecular Screening 4:193-	Hodgkin"s disease), and/or as
	204 (1999); Rowland et al.,	described below under
,	"Lymphocytes: a practical	"Hyperproliferative
	approach" Chapter 6:138-160	Disorders"). Highly preferred
	(2000); and Ye et al., J Leukoc	indications include neoplasms
	Biol (58(2):225-233, the	and cancers, such as, leukemia,
	contents of each of which are	lymphoma, melanoma, and
	herein incorporated by	prostate, breast, lung, colon,
	reference in its entirety.	pancreatic, esophageal,
	Natural killer cells that may be	stomach, brain, liver and
	used according to these assays	urinary cancer. Other preferred
	are publicly available (e.g.,	indications include benign
	through the ATCC) or may be	dysproliferative disorders and
	isolated using techniques	pre-neoplastic conditions, such
	disclosed herein or otherwise	as, for example, hyperplasia,
	known in the art. Natural	metaplasia, and/or dysplasia.
	killer (NK) cells are large	Highly preferred indications
	granular lymphocytes that have	include: suppression of
	cytotoxic activity but do bind	immune reactions to
	antigen. NK cells show	transplanted organs and tissues
	antibody-independent killing	(e.g., bone marrow transplant);
	of tumor cells and also	accelerating myeloid recovery;
	recognize antibody bound on	and mobilizing hematopoietic
	target cells, via NK Fc	progenitor cells. Preferred
	receptors, leading to cell-	indications include boosting a
	mediated cytotoxicity.	T cell-mediated immune

	insulin production. The	disease and nerve damage
	DMEFI response element is	(e.g., due to diabetic
	present in the GLUT4	neuropathy), blood vessel
	promoter and binds to MEF2	blockage, heart disease, stroke,
	transcription factor and another	impotence (e.g., due to diabetic
	transcription factor that is	neuropathy or blood vessel
	required for insulin regulation	blockage), seizures, mental
	of Glut4 expression in skeletal	confusion, drowsiness,
	muscle. GLUT4 is the primary	nonketotic hyperglycemic-
	insulin-responsive glucose	hyperosmolar coma,
	transporter in fat and muscle	cardiovascular disease (e.g.,
	tissue. Exemplary assays that	heart disease, atherosclerosis,
	may be used or routinely	microvascular disease,
	modified to test for DMEF1	hypertension, stroke, and other
	response element activity (in	diseases and disorders as
	adipocytes and pre-adipocytes)	described in the
	by polypeptides of the	"Cardiovascular Disorders"
	invention (including antibodies	section below), dyslipidemia,
	and agonists or antagonists of	endocrine disorders (as
	the invention) include assays	described in the "Endocrine
	disclosed in Thai, M.V., et al., J	Disorders" section below),
-	Biol Chem, 273(23):14285-92	neuropathy, vision impairment
	(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
	Chem, 275(21):16323-8	blindness), ulcers and impaired
	(2000); Liu, M.L., et al., J Biol	wound healing, and infection
	Chem, 269(45):28514-21	(e.g., infectious diseases and
	(1994); "Identification of a 30-	disorders as described in the
	base pair regulatory element	"Infectious Diseases" section
	and novel DNA binding	below, especially of the
	protein that regulates the	urinary tract and skin). An
	human GLUT4 promoter in	additional highly preferred

indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for
transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell
	Activation of Endothelial Cell p38 or JNK
	542
	HAMGG68

	Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell	
		apoptosis are well known in	growth. An alternative highly	
		the art and may be used or	preferred embodiment of the	
		routinely modified to assess	invention includes a method	
		the ability of polypeptides of	for inhibiting endothelial cell	
		the invention (including	growth. A highly preferred	
		antibodies and agonists or	embodiment of the invention	
		antagonists of the invention) to	includes a method for	-
		promote or inhibit cell	stimulating endothelial cell	
		proliferation, activation, and	proliferation. An alternative	
		apoptosis. Exemplary assays	highly preferred embodiment	
	-	for JNK and p38 kinase	of the invention includes a	
		activity that may be used or	method for inhibiting	
-		routinely modified to test JNK	endothelial cell proliferation.	
-		and p38 kinase-induced	A highly preferred	
		activity of polypeptides of the	embodiment of the invention	
		invention (including antibodies	includes a method for	
		and agonists or antagonists of	stimulating apoptosis of	
		the invention) include the	endothelial cells. An	
		assays disclosed in Forrer et	alternative highly preferred	
		al., Biol Chem 379(8-9):1101-	embodiment of the invention	
		1110 (1998); Gupta et al., Exp	includes a method for	
-		Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)	
		(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.	
		Soc Symp 64:29-48 (1999);	A highly preferred	
		Chang and Karin, Nature	embodiment of the invention	
		410(6824):37-40 (2001); and	includes a method for	
		Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)	
		Biol 71(3-4):479-500 (1999);	endothelial cell activation. An	
		the contents of each of which	alternative highly preferred	
		are herein incorporated by	embodiment of the invention	

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includes a method for	inhibiting (e.g., decreasing) the	activation of and/or	inactivating endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular
reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.													,	
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dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications
																		_									-	_		
		_																					-						- 12	
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							_																							

		include neoplasms and cancer,
		such as, Kaposi's sarcoma,
-		cavernous), glomus tumors,
		telangiectasia, bacillary
-		angiomatosis,
		hemangioendothelioma,
		angiosarcoma,
		haemangiopericytoma,
		lymphangioma,
		lymphangiosarcoma. Highly
		preferred indications also
		include cancers such as,
		prostate, breast, lung, colon,
		pancreatic, esophageal,
		stomach, brain, liver, and
		urinary cancer. Preferred
		indications include benign
		dysproliferative disorders and
		pre-neoplastic conditions, such
		as, for example, hyperplasia,
		metaplasia, and/or dysplasia.
		Highly preferred indications
		also include arterial disease,
		such as, atherosclerosis,
		hypertension, coronary artery
		disease, inflammatory
	-	vasculitides, Reynaud"s
		disease and Reynaud's
-		phenomenom, aneurysms,
		restenosis; venous and

lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as	peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured	tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease renal	diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions.
			•

					Additional highly preferred
					indications include fibromas,
_					heart disease, cardiac arrest,
					heart valve disease, and
					vascular disease.
					Preferred indications include
					blood disorders (e.g., as
					described below under
					"Immune Activity", "Blood-
					Related Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
<u>-</u>					preferred indications include
					inflammation and
					inflammatory disorders (such
-					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
HAMGG68	iG68	542	Production of	Endothelial cells, which are	Highly preferred indications
-		-	ICAM in	cells that line blood vessels,	include inflammation (acute
			endothelial cells	and are involved in functions	and chronic), restnosis,
			(such as human	that include, but are not limited	atherosclerosis, asthma and

						_																							
allergy. Highly preferred	indications include	inflammation and	inflammatory disorders,	immunological disorders,	neoplastic disorders (e.g.	cancer/tumorigenesis), and	cardiovascular disorders (such	as described below under	"Immune Activity", "Blood-	Related Disorders",	"Hyperproliferative Disorders"	and/or "Cardiovascular	Disorders"). Highly preferred	indications include neoplasms	and cancers such as, for	example, leukemia, lymphoma,	melanoma, renal cell	carcinoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.		
to, angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.	Exemplary endothelial cells	that may be used in ICAM	production assays include	human umbilical vein	endothelial cells (HUVEC),	and are available from	commercial sources. The	expression of ICAM (CD54),a	intergral membrane protein,	can be upregulated by	cytokines or other factors, and	ICAM expression is important	in mediating immune and	endothelial cell interactions	leading to immune and	inflammatory responses.	Assays for measuring	expression of ICAM-1 are	well-known in the art and may	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate ICAM-1	expression. Exemplary assays	that may be used or routinely
umbilical vein	endothelial cells	(HUVEC))																											
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				disclosed in Rolfe BF et al	
				A thomas 1 40(1), 00 ali.	-
				Ameroscierosis, 149(1):99-110	
		_		(2000); Panettieri RA Jr, et al.,	
				J Immunol, 154(5):2358-2365	
				(1995); and, Grunstein MM, et	
				al., Am J Physiol Lung Cell	
_				Mol Physiol, 278(6):L1154-	
				L1163 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	
				entirety.	
	HAMGR28	543	Stimulation of	Assays for measuring calcium	A highly preferred
			Calcium Flux in	flux are well-known in the art	indication is diabetes mellitus.
			pancreatic beta	and may be used or routinely	An additional highly preferred
			cells.	modified to assess the ability	indication is a complication
				of polypeptides of the	associated with diabetes (e.g.,
				invention (including antibodies	diabetic retinopathy, diabetic
				and agonists or antagonists of	nephropathy, kidney disease
				the invention) to mobilize	(e.g., renal failure,
				calcium. For example, the	nephropathy and/or other
				FLPR assay may be used to	diseases and disorders as
				measure influx of calcium.	described in the "Renal
				Cells normally have very low	Disorders" section below),
				concentrations of cytosolic	diabetic neuropathy, nerve
				calcium compared to much	disease and nerve damage
				higher extracellular calcium.	(e.g., due to diabetic
				Extracellular factors can cause	neuropathy), blood vessel
				an influx of calcium, leading to	blockage, heart disease, stroke,
				activation of calcium	impotence (e.g., due to diabetic
				responsive signaling pathways	neuropathy or blood vessel

and alterations in cell	blockage), seizures, mental
 functions. Exemplary assays	confusion, drowsiness,
that may be used or routinely	nonketotic hyperglycemic-
modified to measure calcium	hyperosmolar coma,
flux by polypeptides of the	cardiovascular disease (e.g.,
invention (including antibodies	heart disease, atherosclerosis,
and agonists or antagonists of	microvascular disease,
 the invention) include assays	hypertension, stroke, and other
 disclosed in: Satin LS, et al.,	diseases and disorders as
Endocrinology, 136(10):4589-	described in the
601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
Endocrinology, 136(7):2960-6	section below), dyslipidemia,
(1995); Richardson SB, et al.,	endocrine disorders (as
 Biochem J, 288 (Pt 3):847-51	described in the "Endocrine
(1992); and, Meats, JE, et al.,	Disorders" section below),
Cell Calcium 1989 Nov-	neuropathy, vision impairment
Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
 contents of each of which is	blindness), ulcers and impaired
 herein incorporated by	wound healing, and infection
 reference in its entirety.	(e.g., infectious diseases and
Pancreatic cells that may be	disorders as described in the
used according to these assays	"Infectious Diseases" section
 are publicly available (e.g.,	below, especially of the
 through the ATCC) and/or	urinary tract and skin), carpal
may be routinely generated.	tunnel syndrome and
Exemplary pancreatic cells that	Dupuytren's contracture).
may be used according to these	An additional highly preferred
assays include HITT15 Cells.	indication is obesity and/or
HITT15 are an adherent	complications associated with
epithelial cell line established	obesity. Additional highly
from Syrian hamster islet cells	preferred indications include

			transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78:	weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
HAPOM49	544	Regulation of viability and proliferation of pancreatic beta cells.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel
			viability assay measures the number of viable cells in culture based on quantitation of the ATP present which	disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke,

				ray induced rat transplantable insulinoma. These cells retain	obesity. Additional highly preferred indications include
				characteristics typical of native	weight loss or alternatively,
				pancreatic beta cells including	weight gain. Additional highly
				glucose inducible insulin	preferred indications are
				secretion. References: Asfari	complications associated with
				et al. Endocrinology 1992	insulin resistance.
11	COLING			130:167.	
HAP	HAPPW30	545	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
		-	Signaling Pathway.	transduction that regulate cell	described below under
				proliferation, activation, or	"Hyperproliferative
				apoptosis are well known in	Disorders"), blood disorders
-				the art and may be used or	(e.g., as described below under
				routinely modified to assess	"Immune Activity",
				the ability of polypeptides of	"Cardiovascular Disorders",
				the invention (including	and/or "Blood-Related
				antibodies and agonists or	Disorders"), and infection
				antagonists of the invention) to	(e.g., an infectious disease as
	-	_		promote or inhibit immune cell	described below under
-		-		(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
				activation, and apoptosis.	preferred indications include
				Exemplary assays for JNK and	autoimmune diseases (e.g.,
				p38 kinase activity that may be	rheumatoid arthritis, systemic
				used or routinely modified to	lupus erythematosis, multiple
				test JNK and p38 kinase-	sclerosis and/or as described
				induced activity of	below) and
				polypeptides of the invention	immunodeficiencies (e.g., as
				(including antibodies and	described below). Additional
				agonists or antagonists of the	highly preferred indications
				invention) include the assays	include inflammation and

	1-in I at many at Diel	4
	disclosed in Folfer et al., Biol	initammatory disorders.
	Chem 379(8-9):1101-1110	Highly preferred indications
	(1998); Gupta et al., Exp Cell	also include neoplastic
	Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
	Symp 64:29-48 (1999); Chang	below under
	and Karin, Nature	"Hyperproliferative
	410(6824):37-40 (2001); and	Disorders"). Highly preferred
	Cobb MH, Prog Biophys Mol	indications include neoplasms
	Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
	the contents of each of which	lymphoma, prostate, breast,
	are herein incorporated by	lung, colon, pancreatic,
-	reference in its entirety. T	esophageal, stomach, brain,
	cells that may be used	liver, and urinary cancer. Other
	according to these assays are	preferred indications include
	publicly available (e.g.,	benign dysproliferative
-	through the ATCC).	disorders and pre-neoplastic
	Exemplary mouse T cells that	conditions, such as, for
	may be used according to these	example, hyperplasia,
	assays include the CTLL cell	metaplasia, and/or dysplasia.
	line, which is an IL-2	Preferred indications include
	dependent suspension-culture	arthritis, asthma, AIDS,
	cell line with cytotoxic	allergy, anemia, pancytopenia,
	activity.	leukopenia, thrombocytopenia,
		Hodgkin"s disease, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt"s lymphoma,
		granulomatous disease,
		inflammatory bowel disease,
		sepsis, psoriasis, suppression

					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HATBR65	546	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
			-	IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
		-		proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
. •				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
		-		known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
				assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic
				(including antibodies and	lupus erythematosis, multiple
				agonists or antagonists of the	sclerosis and/or as described
				invention) to mediate	below) and

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immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response	and alternatively suppressing a	B cell-mediated immune	response. Highly preferred	indications include	inflammation and	inflammatory	disorders.Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myeloma, plasmacytoma,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, myeloma,	plasmacytoma, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign
immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and	the stimulation and	upregulation of T cell	proliferation and functional	activities. Such assays that	may be used or routinely	modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Verhasselt et al., J	Immunol 158:2919-2925	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these
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				assays may be isolated using	dysproliferative disorders and
				techniques disclosed herein or	pre-neoplastic conditions, such
				otherwise known in the art.	as, for example, hyperplasia,
				Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
			-	and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
		-			suppression of immune
			٠		reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
		-			diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
-	HATBR65	546	Regulation of	Assays for the regulation of	A highly preferred
			transcription of	transcription of Malic Enzyme	indication is diabetes mellitus.
			Malic Enzyme in	are well-known in the art and	An additional highly preferred
			adipocytes	may be used or routinely	indication is a complication
				modified to assess the ability	associated with diabetes (e.g.,

invention (including antibodies nephropathy, kidney disease and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, diseases and disorders as a key enzyme in lipogenesis. Malic enzyme is involved in Disorders' section below)
invention (including antibod and agonists or antagonists of the invention) to regulate transcription of Malic Enzym a key enzyme in lipogenesis. Malic enzyme is involved in lipogenesisantipogenesisantipogenesisantipogenesisantipogenesisantipogenesisantipogenesis
invention (in and agonists the invention transcription a key enzyme Malic enzyme lipogenesisal stimulted by
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			Biol Chem, 274(25):17997-	blindness), ulcers and impaired
			8004 (1999); Ijpenberg, A., et	wound healing, and infection
			al., J Biol Chem,	(e.g., infectious diseases and
			272(32):20108-20117 (1997);	disorders as described in the
			Berger, et al., Gene 66:1-10	"Infectious Diseases" section
		10° K	(1988); and, Cullen, B., et al.,	below, especially of the
			Methods in Enzymol.	urinary tract and skin), carpal
			216:362–368 (1992), the	tunnel syndrome and
			contents of each of which is	Dupuytren's contracture).
			herein incorporated by	An additional highly preferred
 		_	reference in its entirety.	indication is obesity and/or
			Hepatocytes that may be used	complications associated with
			according to these assays are	obesity. Additional highly
			publicly available (e.g.,	preferred indications include
			through the ATCC) and/or	weight loss or alternatively,
			may be routinely generated.	weight gain. Aditional
			Exemplary hepatocytes that	highly preferred indications are
			may be used according to these	complications associated with
			assays includes the H4IIE rat	insulin resistance.
			liver hepatoma cell line.	
 HATCB92	547	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as T-cells).	routinely modified to assess	preferred embodiment of the
			the ability of polypeptides of	invention includes a method
			the invention (including	for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate the serum response	indications include blood

		factors and modulate the	disorders (e.g. as described
		expression of genes involved	below under "Immine
		in growth. Exemplary assays	Activity". "Blood-Related
		for transcription through the	Disorders", and/or
		SRE that may be used or	"Cardiovascular Disorders"),
		routinely modified to test SRE	Highly preferred indications
		activity of the polypeptides of	include autoimmune diseases
		the invention (including	(e.g., rheumatoid arthritis,
		antibodies and agonists or	systemic lupus erythematosis,
		antagonists of the invention)	Crohn"s disease, multiple
	3	include assays disclosed in	sclerosis and/or as described
		Berger et al., Gene 66:1-10	below), immunodeficiencies
		(1998); Cullen and Malm,	(e.g., as described below),
		Methods in Enzymol 216:362-	boosting a T cell-mediated
		368 (1992); Henthorn et al.,	immune response, and
		Proc Natl Acad Sci USA	suppressing a T cell-mediated
		85:6342-6346 (1988); and	immune response. Additional
		Black et al., Virus Genes	highly preferred indications
		12(2):105-117 (1997), the	include inflammation and
		content of each of which are	inflammatory disorders, and
		herein incorporated by	treating joint damage in
		reference in its entirety. T	patients with rheumatoid
•	•	cells that may be used	arthritis. An additional highly
		according to these assays are	preferred indication is sepsis.
		publicly available (e.g.,	Highly preferred indications
		through the ATCC).	include neoplastic diseases
		Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
		may be used according to these	and/or as described below
		assays include the CTLL cell	under "Hyperproliferative
	-	line, which is an IL-2	Disorders"). Additionally,
		dependent suspension culture	highly preferred indications

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include neoplasms and cancers, such as, for example	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis.
of T cells with cytotoxic activity.																													
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HATEE46	548	Activation of Endothelial Cell p38 or JNK	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell	meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). A highly preferred embodiment of the invention includes a method for	
		Signaling Pathway.	proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase	stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a	
			activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-	method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention	

(1998)	1110 (1998): Gupta et al., Exp	includes a method for
 Cell Res 2	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
 (1999); Ky	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
 Soc Symp	Soc Symp 64:29-48 (1999);	A highly preferred
Chang and	Chang and Karin, Nature	embodiment of the invention
410(6824)	410(6824):37-40 (2001); and	includes a method for
 Cobb MH,	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
 Biol 71(3-	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
 the content	the contents of each of which	alternative highly preferred
are herein	are herein incorporated by	embodiment of the invention
reference i	reference in its entirety.	includes a method for
Endothelia	Endothelial cells that may be	inhibiting (e.g., decreasing) the
 used accor	used according to these assays	activation of and/or
are public	are publicly available (e.g.,	inactivating endothelial cells.
through the ATCC).	e ATCC).	A highly preferred
Exemplary	Exemplary endothelial cells	embodiment of the invention
that may b	that may be used according to	includes a method for
these assay	these assays include human	stimulating angiogenisis. An
umbilical	umbilical vein endothelial cells	alternative highly preferred
(HUVEC),	(HUVEC), which are	embodiment of the invention
endothelia	endothelial cells which line	includes a method for
venous blo	venous blood vessels, and are	inhibiting angiogenesis. A
involved in	involved in functions that	highly preferred embodiment
 include, bu	include, but are not limited to,	of the invention includes a
angiogene	angiogenesis, vascular	method for reducing cardiac
permeabili	permeability, vascular tone,	hypertrophy. An alternative
and immu	and immune cell extravasation.	highly preferred embodiment
		of the invention includes a
		method for inducing cardiac
		hypertrophy. Highly
		preferred indications include

neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atheroselerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	etimilate anciocanacia and/or
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cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,
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metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis,	disease, inflammatory vasculitides, Reynaud's disease and Reynaud's	restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and	lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly	preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as injury resulting from	balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury,	cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred
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					inflammatory disorders (such
					as acute and chronic
_					inflammatory diseases, e.g.,
					inflammatory bowel disease
_					and Crohn's disease), and pain
					management.
	HATEE46	548	Production of	Assays for measuring	Preferred embodiments of the
			ICAM-1	expression of ICAM-1 are	invention include using
				well-known in the art and may	polypeptides of the invention
				be used or routinely modified	(or antibodies, agonists, or
•				to assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				(including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	Inflammation, Vascular
				invention) to regulate ICAM-1	Disease, Athereosclerosis,
				expression. Exemplary assays	Restenosis, and Stroke
_				that may be used or routinely	
				modified to measure ICAM-1	
				expression include assays	
_				disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281	
				(2001); and, Miyamoto K, et	
				al., Am J Pathol, 156(5):1733-	
				1739 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	
				entirety. Cells that may be	
				used according to these assays	
				are publicly available (e.g.,	
				through the ATCC) and/or	
				may be routinely generated.	

				Exemplary cells that may be	
				used according to these assays	
				include microvascular	
				endothelial cells (MVEC).	
	HAUAI83	549	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
				of insulin are well-known in	is diabetes mellitus. An
				the art and may be used or	additional highly preferred
				routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
			_	antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
-				anti-rat insulin antibodies.	Disorders" section below),
				Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
				upregulated by glucose and	(e.g., due to diabetic
				also by certain	neuropathy), blood vessel
				proteins/peptides, and	blockage, heart disease, stroke,
				disregulation is a key	impotence (e.g., due to diabetic
				component in diabetes.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
_				test for stimulation of insulin	nonketotic hyperglycemic-
				secretion (from pancreatic	hyperosmolar coma,
				cells) by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,
				the invention) include assays	hypertension, stroke, and other

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	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional highly	preferred indications are	complications associated with	insulin resistance.			
	disclosed in: Shimizu, H., et	al., Endocr J, 47(3):261-9	(2000); Salapatek, A.M., et al.,	Mol Endocrinol, 13(8):1305-	17 (1999); Filipsson, K., et al.,	Ann N Y Acad Sci, 865:441-4	(1998); Olson, L.K., et al., J	Biol Chem, 271(28):16544-52	(1996); and, Miraglia S et. al.,	Journal of Biomolecular	Screening, 4:193-204 (1999),	the contents of each of which	is herein incorporated by	reference in its entirety.	Pancreatic cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary pancreatic cells that	may be used according to these	assays include HITT15 Cells.	HITT15 are an adherent	epithelial cell line established	from Syrian hamster islet cells	transformed with SV40. These	cells express glucagon,	somatostatin, and	glucocorticoid receptors. The	cells secrete insulin, which is	
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	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy, or blood vessel	blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma,
glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key	Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic
	Stimulation of insulin secretion from pancreatic beta cells.	
	HBAMB15 : 550	
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cells) by nolypeptides of the	cardiovascular disease (e o
 invention (including antibodies	heart disease, atherosclerosis,
and agonists or antagonists of	microvascular disease,
the invention) include assays	hypertension, stroke, and other
disclosed in: Ahren, B., et al.,	diseases and disorders as
Am J Physiol, 277(4 Pt	described in the
2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
 al., Endocrinology,	section below), dyslipidemia,
138(9):3735-40 (1997); Kim,	endocrine disorders (as
K.H., et al., FEBS Lett,	described in the "Endocrine
377(2):237-9 (1995); and,	Disorders" section below),
Miraglia S et. al., Journal of	neuropathy, vision impairment
Biomolecular Screening,	(e.g., diabetic retinopathy and
4:193-204 (1999), the contents	blindness), ulcers and impaired
 of each of which is herein	wound healing, and infection
 incorporated by reference in its	(e.g., infectious diseases and
entirety. Pancreatic cells that	disorders as described in the
may be used according to these	"Infectious Diseases" section
assays are publicly available	below, especially of the
(e.g., through the ATCC)	urinary tract and skin), carpal
and/or may be routinely	tunnel syndrome and
 generated. Exemplary	Dupuytren's contracture).
pancreatic cells that may be	An additional highly preferred
used according to these assays	indication is obesity and/or
include rat INS-1 cells. INS-1	complications associated with
cells are a semi-adherent cell	obesity. Additional highly
 line established from cells	preferred indications include
isolated from an X-ray induced	weight loss or alternatively,
rat transplantable insulinoma.	weight gain. Aditional
These cells retain	highly preferred indications are
characteristics typical of native	complications associated with

				pancreatic beta cells including	insulin resistance.
				glucose inducible insulin	
				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:167.	
	HBGBA69	551	Regulation of	Assays for the regulation of	A highly preferred indication
			viability and	viability and proliferation of	is diabetes mellitus. An
			proliferation of	cells in vitro are well-known in	additional highly preferred
			pancreatic beta	the art and may be used or	indication is a complication
			cells.	routinely modified to assess	associated with diabetes (e.g.,
				the ability of polypeptides of	diabetic retinopathy, diabetic
				the invention (including	nephropathy, kidney disease
				antibodies and agonists or	(e.g., renal failure,
				antagonists of the invention) to	nephropathy and/or other
				regulate viability and	diseases and disorders as
				proliferation of pancreatic beta	described in the "Renal
				cells. For example, the Cell	Disorders" section below),
				Titer-Glo luminescent cell	diabetic neuropathy, nerve
				viability assay measures the	disease and nerve damage
				number of viable cells in	(e.g., due to diabetic
				culture based on quantitation	neuropathy), blood vessel
				of the ATP present which	blockage, heart disease, stroke,
				signals the presence of	impotence (e.g., due to diabetic
				metabolically active cells.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
,				used or routinely modified to	confusion, drowsiness,
				test regulation of viability and	nonketotic hyperglycemic-
				proliferation of pancreatic beta	hyperosmolar coma,
				cells by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,

				the invention) include assays	hypertension, stroke, and other	
_				disclosed in: Friedrichsen BN,	diseases and disorders as	
				et al., Mol Endocrinol,	described in the	
				15(1):136-48 (2001); Huotari	"Cardiovascular Disorders"	
				MA, et al., Endocrinology,	section below), dyslipidemia,	
 -				139(4):1494-9 (1998); Hugl	endocrine disorders (as	
				SR, et al., J Biol Chem 1998	described in the "Endocrine	
				Jul 10;273(28):17771-9	Disorders" section below),	
				(1998), the contents of each of	neuropathy, vision impairment	
				which is herein incorporated	(e.g., diabetic retinopathy and	
				by reference in its entirety.	blindness), ulcers and impaired	
				Pancreatic cells that may be	wound healing, and infection	
				used according to these assays	(e.g., infectious diseases and	
				are publicly available (e.g.,	disorders as described in the	
				through the ATCC) and/or	"Infectious Diseases" section	
				may be routinely generated.	below, especially of the	
				Exemplary pancreatic cells that	urinary tract and skin), carpal	
				may be used according to these	tunnel syndrome and	
				assays include rat INS-1 cells.	Dupuytren's contracture). An	
				INS-1 cells are a semi-	additional highly preferred	
				adherent cell line established	indication is obesity and/or	
				from cells isolated from an X-	complications associated with	
				ray induced rat transplantable	obesity. Additional highly	
¥ 1 € 1				insulinoma. These cells retain	preferred indications include	
				characteristics typical of native	weight loss or alternatively,	
				pancreatic beta cells including	weight gain. Additional highly	
	-	-		glucose inducible insulin	preferred indications are	
				secretion. References: Asfari	complications associated with	
	_			et al. Endocrinology 1992 130:167.	insulin resistance.	
HBGBA69		551	VEGF in SW480			

	HBIAE26	552	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
				of insulin are well-known in	is diabetes mellitus. An
				the art and may be used or	additional highly preferred
-				routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
	-			Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
				upregulated by glucose and	(e.g., due to diabetic
				also by certain	neuropathy), blood vessel
				proteins/peptides, and	blockage, heart disease, stroke,
				disregulation is a key	impotence (e.g., due to diabetic
				component in diabetes.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
				test for stimulation of insulin	nonketotic hyperglycemic-
				secretion (from pancreatic	hyperosmolar coma,
				cells) by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,
				the invention) include assays	hypertension, stroke, and other
				disclosed in: Shimizu, H., et	diseases and disorders as
				al., Endocr J, 47(3):261-9	described in the
				(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
				Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,

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endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional highly	preferred indications are	complications associated with	insulin resistance.							
17 (1999); Filipsson, K., et al.,	Ann N Y Acad Sci, 865:441-4	(1998); Olson, L.K., et al., J	Biol Chem, 271(28):16544-52	(1996); and, Miraglia S et. al.,	Journal of Biomolecular	Screening, 4:193-204 (1999),	the contents of each of which	is herein incorporated by	reference in its entirety.	Pancreatic cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary pancreatic cells that	may be used according to these	assays include HITT15 Cells.	HITT15 are an adherent	epithelial cell line established	from Syrian hamster islet cells	transformed with SV40. These	cells express glucagon,	somatostatin, and	glucocorticoid receptors. The	cells secrete insulin, which is	stimulated by glucose and	glucagon and suppressed by	somatostatin or	glucocorticoids. ATTC# CRL-	1777 Refs: Lord and
		-				-1					-				-		de para													

				Ashcroff Biochem I 219.	
-				547-551; Santerre et al. Proc.	
				Natl. Acad. Sci. USA 78:	
				4339-4343, 1981.	
	HBJNC59	554	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
			Signaling Pathway.	transduction that regulate cell	described below under
				proliferation, activation, or	"Hyperproliferative
				apoptosis are well known in	Disorders"), blood disorders
				the art and may be used or	(e.g., as described below under
				routinely modified to assess	"Immune Activity",
				the ability of polypeptides of	"Cardiovascular Disorders",
				the invention (including	and/or "Blood-Related
				antibodies and agonists or	Disorders"), and infection
				antagonists of the invention) to	(e.g., an infectious disease as
				promote or inhibit immune cell	described below under
				(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
-				activation, and apoptosis.	preferred indications include
				Exemplary assays for JNK and	autoimmune diseases (e.g.,
				p38 kinase activity that may be	rheumatoid arthritis, systemic
				used or routinely modified to	lupus erythematosis, multiple
				test JNK and p38 kinase-	sclerosis and/or as described
				induced activity of	below) and
				polypeptides of the invention	immunodeficiencies (e.g., as
				(including antibodies and	described below). Additional
				agonists or antagonists of the	highly preferred indications
				invention) include the assays	include inflammation and
	-			disclosed in Forrer et al., Biol	inflammatory disorders.
				Chem 379(8-9):1101-1110	Highly preferred indications
				(1998); Gupta et al., Exp Cell	also include neoplastic
				Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,

											-													_						_
A preferred embodiment of	the invention includes a	method for inhibiting (e.g.,	reducing) TNF alpha	production. An alternative	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) TNF alpha	production. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	1
Assays for the activation of	transcription through the	Serum Response Element	(SRE) are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate the serum response	factors and modulate the	expression of genes involved	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	Santonia of and a Contraction of
Activation of	transcription	through serum	response element in	immune cells (such	as T-cells).																									
555																														
HBNAW17										_																				
		_					-				-																			

		herein incomorated by	treating joint damage in
		information in the partition.	
		reference in its entirety.	patients with rheumatoid
		cells that may be used	arthritis. An additional highly
		according to these assays are	preferred indication is sepsis.
		publicly available (e.g.,	Highly preferred indications
		through the ATCC).	include neoplastic diseases
		Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
		may be used according to these	and/or as described below
		assays include the CTLL cell	under "Hyperproliferative
		line, which is an IL-2	Disorders"). Additionally,
		dependent suspension culture	highly preferred indications
		of T cells with cytotoxic	include neoplasms and
	.,	activity.	cancers, such as, for example,
			leukemia, lymphoma,
			melanoma, glioma (e.g.,
-			malignant glioma), solid
			tumors, and prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
			example, hyperplasia,
			metaplasia, and/or dysplasia.
			Preferred indications include
			anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
			lymphocytic anemia (ALL),

				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS, granulomatous
				disease, inflammatory bowel
				disease, neutropenia,
			-	neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
				cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication
				is infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
HBNAWI7	555	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
			of insulin are well-known in	is diabetes mellitus. An
			the art and may be used or	additional highly preferred
			routinely modified to assess	indication is a complication
			the ability of polypeptides of	associated with diabetes (e.g.,
			the invention (including	diabetic retinopathy, diabetic
			antibodies and agonists or	nephropathy, kidney disease
			antagonists of the invention) to	(e.g., renal failure,
			stimulate insulin secretion.	nephropathy and/or other
			For example, insulin secretion	diseases and disorders as
	•		is measured by FMAT using	described in the "Renal
			anti-rat insulin antibodies.	Disorders" section below),
			Insulin secretion from	diabetic neuropathy, nerve

	pancreatic beta cells is	disease and nerve damage
	upregulated by glucose and	(e.g., due to diabetic
	also by certain	neuropathy), blood vessel
	proteins/peptides, and	blockage, heart disease, stroke,
	disregulation is a key	impotence (e.g., due to diabetic
	component in diabetes.	neuropathy or blood vessel
	Exemplary assays that may be	blockage), seizures, mental
	used or routinely modified to	confusion, drowsiness,
	test for stimulation of insulin	nonketotic hyperglycemic-
	secretion (from pancreatic	hyperosmolar coma,
	cells) by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
-	the invention) include assays	hypertension, stroke, and other
	disclosed in: Shimizu, H., et	diseases and disorders as
	al., Endocr J, 47(3):261-9	described in the
	(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
	Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
	17 (1999); Filipsson, K., et al.,	endocrine disorders (as
	Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
	(1998); Olson, L.K., et al., J	Disorders" section below),
	Biol Chem, 271(28):16544-52	neuropathy, vision impairment
	(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
	Journal of Biomolecular	blindness), ulcers and impaired
	Screening, 4:193-204 (1999),	wound healing, and infection
	the contents of each of which	(e.g., infectious diseases and
	is herein incorporated by	disorders as described in the
	reference in its entirety.	"Infectious Diseases" section
	Pancreatic cells that may be	below, especially of the
	used according to these assays	urinary tract and skin), carpal
	are publicly available (e.g.,	tunnel syndrome and

			through the ATCC) and/or may be routinely generated	Dupuytren's contracture).
			Exemplary pancreatic cells that	indication is obesity and/or
			may be used according to these	complications associated with
			assays include HITT15 Cells.	obesity. Additional highly
			HITT15 are an adherent	preferred indications include
			epithelial cell line established	weight loss or alternatively,
			from Syrian hamster islet cells	weight gain. Additional highly
			transformed with SV40. These	preferred indications are
			cells express glucagon,	complications associated with
-			somatostatin, and	insulin resistance.
			glucocorticoid receptors. The	
-			cells secrete insulin, which is	
			stimulated by glucose and	
			glucagon and suppressed by	
			somatostatin or	
			glucocorticoids. ATTC# CRL-	
			1777 Refs: Lord and	
			Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc.	
-			Natl. Acad. Sci. USA 78:	
			4339-4343, 1981.	
HBOEG69	556	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as natural killer	routinely modified to assess	highly preferred embodiment
		cells).	the ability of polypeptides of	of the invention includes a
			the invention (including	method for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha

		Exemplary T cells that may be	Disorders"). Additionally,
		used according to these assays	highly preferred indications
		include the NK-YT cell line,	include neoplasms and
	•	which is a human natural killer	cancers, such as, for example,
		cell line with cytolytic and	leukemia, lymphoma,
		cytotoxic activity.	melanoma, glioma (e.g.,
			malionant olioma) solid
			tumose and mostate become
			tumors, and prostate, breast,
		-	lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
P			example, hyperplasia,
			metaplasia, and/or dysplasia.
			Preferred indications include
			anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
	-		lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
			disease, inflammatory bowel
			disease, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted
			organs and tissues, hemophilia,

HCACU58	557	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved	hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune
			in growth. Exemplary assays for transcription through the	Activity", "Blood-Related Disorders", and/or
			SRE that may be used or routinely modified to test SRE activity of the polypeptides of	"Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases
			the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in	(e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described

encies	w),	ated		ediated	ditional	tions	pu	, and		p <u>i</u>	highly	sepsis.	tions	ases	ma,	, MO	ive	Illy,	ions		ample,		•	id	east,		rain,	: Other	
nunodefici	cribed belc	l cell-medi	ponse, and	a T cell-m	ponse. Ac	rred indica	ammation s	ry disorder.	t damage i	h rheumato	1 additiona	dication is	erred indica	plastic dise	nia, lympho	scribed bel	erproliferat	Additions	rred indica	lasms and	h as, for ex	mphoma,	ylioma (e.g	ioma), sol	prostate, bi	pancreatic,	stomach, t	nary cance	
below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	
66:1-10	Malm,	ol 216:362-	rn et al.,	USA	8); and	Genes	7), the	which are	by	rety. T	ed	ssays are	.g.,		cells that	ing to these	TLL cell	5	on culture	oxic				-					-
Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety.	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic									
Berger	(1998)	Method	368 (19	Proc N	85:634	Black e	12(2):1	content	herein	referen	cells th	accordi	publicly	through	Exemp	may be	assays i	line, wł	depende	of T cel	activity.								
						·	- <u>-</u>			-			_																_
																				_									-
						- <u>-</u> -				-			-						-								-		_
	-													_						_									

disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune	reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and	asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	easures 'A-3 HMC-1
					This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line
					Activation of transcription through GATA-3 response element in
					557
					HCACU58

	immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
	as mast cells).	cells has been linked to	described below under
		cytokine and chemokine	"Infectious Disease"), and
		production. Assays for the	inflammation and
		activation of transcription	inflammatory disorders.
		through the GATA3 response	Preferred indications also
	-	element are well-known in the	include blood disorders (e.g.,
		art and may be used or	as described below under
		routinely modified to assess	"Immune Activity", "Blood-
		the ability of polypeptides of	Related Disorders", and/or
		the invention (including	"Cardiovascular Disorders").
		antibodies and agonists or	Preferred indications include
		antagonists of the invention) to	autoimmune diseases (e.g.,
		regulate GATA3 transcription	rheumatoid arthritis, systemic
		factors and modulate	lupus erythematosis, multiple
		expression of mast cell genes	sclerosis and/or as described
		important for immune response	below) and
		development. Exemplary	immunodeficiencies (e.g., as
		assays for transcription	described below). Preferred
		through the GATA3 response	indications include neoplastic
		element that may be used or	diseases (e.g., leukemia,
		routinely modified to test	lymphoma, melanoma,
		GATA3-response element	prostate, breast, lung, colon,
		activity of polypeptides of the	pancreatic, esophageal,
		invention (including antibodies	stomach, brain, liver, and
~		and agonists or antagonists of	urinary tract cancers and/or as
		the invention) include assays	described below under
		disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Malm, Methods in Enzymol	indications include benign
		216:362-368 (1992); Henthorn	dysproliferative disorders and

				et al Proc Natl Acad Sci USA	nre-neonlastic conditions such
_				85:6342-6346 (1988); Flavell	as. for example, hyperplasia
				et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia
				Quant Biol 64:563-571 (1999);	Preferred indications include
		_		Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
				J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
				(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
				Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
				Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
				14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
_				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HCACU58	557	Production of	Endothelial cells, which are	Highly preferred indications
			ICAM in	cells that line blood vessels,	include inflammation (acute
			endothelial cells	and are involved in functions	and chronic), restnosis,
			(such as human	that include, but are not limited	atherosclerosis, asthma and

allergy. Highly preferred indications include inflammation and	inflammatory disorders,	immunological disorders,	neoplastic disorders (e.g.	cancer/tumorigenesis), and	cardiovascular disorders (such	as described below under	"Immune Activity", "Blood-	Related Disorders",	"Hyperproliferative Disorders"	and/or "Cardiovascular	Disorders"). Highly preferred	indications include neoplasms	and cancers such as, for	example, leukemia, lymphoma,	melanoma, renal cell	carcinoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.			
to, angiogenesis, vascular, permeability, vascular tone, and immune cell extravasation.	Exemplary endothelial cells	that may be used in ICAM	production assays include	human umbilical vein	endothelial cells (HUVEC),	and are available from	commercial sources. The	expression of ICAM (CD54),a	intergral membrane protein,	can be upregulated by	cytokines or other factors, and	ICAM expression is important	in mediating immune and	endothelial cell interactions	leading to immune and	inflammatory responses.	Assays for measuring	expression of ICAM-1 are	well-known in the art and may	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate ICAM-1	expression. Exemplary assays	that may be used or routinely	modified to measure ICAM-1
umbilical vein endothelial cells (HUVEC))																							-					
																		-										
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proliferation include, for example, assays such as disclosed and/or cited in: Robinson, DS, et al., "Th-2 cytokines in allergic disease" Br Med Buli; 56 (4): 956-968 (2000), and Cohn, et al., "Th-helper type 2 cell-directed therapy for asthma" Pharmacology & Therapeutics; 88: 187-196 (2000), the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL/IO secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL/II, IL/I3, IL/S and IL/G. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and asthmary T helper 2 cells are generated via in vitro culture under Th2 polarizing																															
	proliferation include, for	example, assays such as	disclosed and/or cited in:	Robinson, DS, et al., "Th-2	cytokines in allergic disease"	Br Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the	contents of each of which are	herein incorporated by	reference in their entirety.	Exemplary cells that may be	used according to these assays	include Th2 cells. IL10	secreted from Th2 cells may be	measured as a marker of Th2	cell activation. Th2 cells are	a class of T cells that secrete	IL4, IL10, IL13, IL5 and IL6.	Factors that induce	differentiation and activation	of Th2 cells play a major role	in the initiation and	pathogenesis of allergy and	asthma. Primary Thelper 2	cells are generated via in vitro	culture under Th2 polarizing	conditions using peripheral

				blood lymphocytes isolated from cord blood.	
HCE2F54	54	558	Regulation of	Assays for the regulation of	A highly preferred
			transcription	transcription through the	indication is diabetes mellitus.
			through the PEPCK	PEPCK promoter are well-	An additional highly preferred
			promoter in	known in the art and may be	indication is a complication
			hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
				assess the ability of	diabetic retinopathy, diabetic
				polypeptides of the invention	nephropathy, kidney disease
				(including antibodies and	(e.g., renal failure,
				agonists or antagonists of the	nephropathy and/or other
				invention) to activate the	diseases and disorders as
				PEPCK promoter in a reporter	described in the "Renal
				construct and regulate liver	Disorders" section below),
-				gluconeogenesis. Exemplary	diabetic neuropathy, nerve
	•			assays for regulation of	disease and nerve damage
	•			transcription through the	(e.g., due to diabetic
				PEPCK promoter that may be	neuropathy), blood vessel
				used or routinely modified to	blockage, heart disease, stroke,
				test for PEPCK promoter	impotence (e.g., due to diabetic
			-	activity (in hepatocytes) of	neuropathy or blood vessel
				polypeptides of the invention	blockage), seizures, mental
				(including antibodies and	confusion, drowsiness,
				agonists or antagonists of the	nonketotic hyperglycemic-
				invention) include assays	hyperosmolar coma,
				disclosed in Berger et al., Gene	cardiovascular disease (e.g.,
				66:1-10 (1998); Cullen and	heart disease, atherosclerosis,
				Malm, Methods in Enzymol	microvascular disease,
				216:362-368 (1992); Henthorn	hypertension, stroke, and other
				et al., Proc Natl Acad Sci USA	diseases and disorders as
				85:6342-6346 (1988);	described in the

"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	an infectious diseases or	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as
Lochhead et al., Diabetes	49(6):896-903 (2000); and	Yeagley et al., J Biol Chem	275(23):17814-17820 (2000),	the contents of each of which	is herein incorporated by	reference in its entirety.	Hepatocyte cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary liver hepatoma	cells that may be used	according to these assays	include H4lle cells, which	contain a tyrosine amino	transferase that is inducible	with glucocorticoids, insulin,	or cAMP derivatives.											
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described herein.	Additional highly preferred	indications include glycogen	storage disease (e.g.,	glycogenoses), hepatitis,	gallstones, cirrhosis of the	liver, degenerative or necrotic	liver disease, alcoholic liver	diseases, fibrosis, liver	regeneration, metabolic	disease, dyslipidemia and	cholesterol metabolism, and	hepatocarcinomas.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), infection	(e.g., an infectious disease	and/or disorder as described	below under "Infectious	Disease"), endocrine disorders	(e.g., as described below under	"Endocrine Disorders"), and	neural disorders (e.g., as	described below under "Neural	Activity and Neurological
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					Diseases").
					Additional preferred
-					indications include neoplastic
					diseases (e.g., as described
					below under
					"Hyperproliferative
					Disorders"). Preferred
					indications include neoplasms
					and cancers, such as, leukemia,
				-	lymphoma, prostate, breast,
					lung, colon, pancreatic,
					esophageal, stomach, brain,
					and urinary cancer. A highly
					preferred indication is liver
					cancer. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
HCE2F54	2F54	558	Activation of	Assays for the activation of	Preferred embodiments of the
			transcription	transcription through the	invention include using
			through NFKB	NFKB response element are	polypeptides of the invention
			response element in	well-known in the art and may	(or antibodies, agonists, or
			epithelial cells	be used or routinely modified	antagonists thereof) in
_			(such as HELA	to assess the ability of	detection, diagnosis,
			cells).	polypeptides of the invention	prevention, and/or treatment of
				(including antibodies and	Cancer, Wound Healing, and
	-			agonists or antagonists of the	Inflamation. Highly preferred
				invention) to regulate NFKB	indications include neoplastic
				transcription factors and	diseases (e.g., as described

below under		Disorders"). Highly preferred			example, melanoma, and	prostate, breast, lung, colon,								3-			inflammatory disorders.			1 9 1	1,						-re			
modulate expression of	epithhelial genes. Exemplary	assays for transcription	through the NFKB response	element that may be used or	routinely modified to test	NFKB-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Kaltschmidt B, et	al., Oncogene, 18(21):3213-	3225 (1999); Beetz A, et al.,	Int J Radiat Biol, 76(11):1443-	1453 (2000); Berger et al.,	Gene 66:1-10 (1998); Cullen	and Malm, Methods in	Enzymol 216:362-368 (1992);	Henthorn et al., Proc Natl	Acad Sci USA 85:6346	(1988); Valle Blazquez et al,	Immunology 90(3):455-460	(1997); Aramburau et al., J	Exp Med 82(3):801-810	(1995); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety.	Epithelial cells that may be
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used according to these assays are publicly available (e.g., through the ATCC). Exemplary epithelial cells that may be used according to these assays include the HELA cell line.	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of
	Inhibition of squalene synthetase gene transcription.	Proliferation of preadipose cells (such as 3T3-L1 cells)
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	HCE2F54	HCE2F54
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cells in vitro are well-known in	the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate viability and	proliferation of pre-adipose	cells and cell lines. For	example, the CellTiter-Gloô	Luminescent Cell Viability	Assay (Promega Corp.,	Madison, WI, USA) can be	used to measure the number of	viable cells in culture based on	quantitation of the ATP	present which signals the	presence of metabolically	active cells. 3T3-L1 is a	mouse preadipocyte cell line. It	is a continuous substrain of	3T3 fibroblast cells developed	through clonal isolation. Cells	were differentiated to an	adipose-like state before being	used in the screen. See Green	H and Meuth M., Cell 3: 127-	133 (1974), which is herein	incorporated by reference in its	entirety.
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This reporter assay measures	activation or inhibition of the	NFkB signaling pathway in	Ku812 human basophil cell	line. Assays for the activation	or inhibition of transcription	through the NFKB response	element are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate NFKB transcription	factors and modulate	expression of	immunomodulatory genes.	NFkB is important in the	pathogenesis of asthma.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene
Activation or	inhibition of	transcription	through NFKB	response element in	immune cells (such	as basophils).																								
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66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone	et al, Int Arch Allergy	Immunol 114(3):207-17	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Cells were pretreated with SID	supernatants or controls for 15-	18 hours, and then 10 ng/mL	of TNF was added to stimulate	the NFkB reporter. SEAP	activity was measured after 48	hours. Basophils that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary human basophil	cell lines that may be used	according to these assays	include Ku812, originally	established from a patient with	chronic myelogenous	leukemia. It is an immature	prebasophilic cell line that can	be induced to differentiate into	mature basophils. See, Kishi et	al., Leuk Res. 9:381-390
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	Highly preferred indications include inflammation and	inflammatory disorders.	Highly preferred indications	hematopoietic disorders (e.g.	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below), and	immunodeficiencies (e.g., as	described below). An	additional highly preferred	indication is infection (e.g.,	AIDS, and/or an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,
(1985); Blom et al., Eur J Immunol. 22:2025-32 (1992), where the contents of each are herein incorporated by reference in its entirety.	This assay uses a NFKB response element (which will	bind NFKB transcription	factors) linked to a reporter	mediated transcription in the	human monocyte cell line	U937. NFKB is upregulated	by cytokines and other factors	and NFKB element activation	leads to expression of	immunomodulatory genes.	Activation of NFKB in	monocytes can play a role in	immune responses. Exemplary	assays for transcription	through the NFKB response	element that may be used or	rountinely modified to test	NFKB-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and
	Activation of transcription	through NFKB	response element in immine cells (such	as the U937 human	monocyte cell line).																			
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	Malm, Methods in Enzymol	lymphoma, and/or as described
	216:362-368 (1992); Henthorn	below under
	et al., Proc Natl Acad Sci USA	"Hyperproliferative
	85:6342-6346 (1988); Valle	Disorders"). Highly preferred
	Blazquez et al, Immunology	indications include neoplasms
	90(3):455-460 (1997);	and cancers, such
	Aramburau et al., J Exp Med	as,melanoma, renal cell
	82(3):801-810 (1995); and	carcinoma, leukemia,
	Fraser et al., 29(3):838-844	lymphoma, and prostate,
	(1999), the contents of each of	breast, lung, colon, pancreatic,
	which are herein incorporated	esophageal, stomach, brain,
	by reference in its entirety.	liver and urinary cancer. Other
	Monocytic cells that may be	preferred indications include
	used according to these assays	benign dysproliferative
	are publicly available (e.g.,	disorders and pre-neoplastic
	through the ATCC).	conditions, such as, for
	Exemplary human monocyte	example, hyperplasia,
	cells that may be used	metaplasia, and/or dysplasia.
	according to these assays	Preferred indications also
-	include the U937 cell line,	include anemia, pancytopenia,
	which is cell line derived by	leukopenia, thrombocytopenia,
	Sundstrom and Nilsson in	Hodgkin's disease, acute
	1974 from malignant cells	lymphocytic anemia (ALL),
-	obtained from the pleural	plasmacytomas, multiple
	effusion of a patient with	myeloma, Burkitt's lymphoma,
	histiocytic lymphoma.	arthritis, AIDS,
-		granulomatous disease,
		inflammatory bowel disease,
		sepsis, neutropenia,
		neutrophilia, psoriasis,
		hemophilia, hypercoagulation,

diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.		
	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or
	Inhibition of squalene synthetase gene transcription.	Proliferation of preadipose cells (such as 3T3-L1 cells)
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				routinely modified to assess the ability of polypeptides of	
				the invention (including	
				antibodies and agonists or	
-				antagonists of the invention) to	
				regulate viability and	
				proliferation of pre-adipose	
				cells and cell lines. For	
				example, the CellTiter-Gloô	
				Luminescent Cell Viability	
				Assay (Promega Corp.,	
				Madison, WI, USA) can be	
				used to measure the number of	
				viable cells in culture based on	
				quantitation of the ATP	
_				present which signals the	
				presence of metabolically	
				active cells. 3T3-L1 is a	
				mouse preadipocyte cell line. It	
				is a continuous substrain of	
				3T3 fibroblast cells developed	
				through clonal isolation. Cells	
				were differentiated to an	
				adipose-like state before being	
				used in the screen. See Green	
				H and Meuth M., Cell 3: 127-	
				133 (1974), which is herein	
				incorporated by reference in its	
				entirety.	
	HCE3G69	559	Stimulation of	Assays for measuring secretion	A highly preferred
			insulin secretion	of insulin are well-known in	indication is diabetes mellitus.

from pancreatic	the art and may be used or	An additional highly preferred
beta cells.	routinely modified to assess	indication is a complication
	the ability of polypeptides of	associated with diabetes (e.g.,
	the invention (including	diabetic retinopathy, diabetic
	antibodies and agonists or	nephropathy, kidney disease
	antagonists of the invention) to	(e.g., renal failure,
	stimulate insulin secretion.	nephropathy and/or other
	For example, insulin secretion	diseases and disorders as
	is measured by FMAT using	described in the "Renal
	anti-rat insulin antibodies.	Disorders" section below),
	Insulin secretion from	diabetic neuropathy, nerve
	pancreatic beta cells is	disease and nerve damage
	upregulated by glucose and	(e.g., due to diabetic
	also by certain	neuropathy), blood vessel
	proteins/peptides, and	blockage, heart disease, stroke,
	disregulation is a key	impotence (e.g., due to diabetic
	component in diabetes.	neuropathy or blood vessel
	Exemplary assays that may be	blockage), seizures, mental
	used or routinely modified to	confusion, drowsiness,
	test for stimulation of insulin	nonketotic hyperglycemic-
	secretion (from pancreatic	hyperosmolar coma,
	cells) by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Ahren, B., et al.,	diseases and disorders as
	Am J Physiol, 277(4 Pt	described in the
	2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
	al., Endocrinology,	section below), dyslipidemia,
	138(9):3735-40 (1997); Kim,	endocrine disorders (as
	K.H., et al., FEBS Lett,	described in the "Endocrine

				377(2):237-9 (1995); and,	Disorders" section below).
				Miraglia S et. al., Journal of	neuropathy, vision impairment
				Biomolecular Screening,	(e.g., diabetic retinopathy and
				4:193-204 (1999), the contents	blindness), ulcers and impaired
				of each of which is herein	wound healing, and infection
	-			incorporated by reference in its	(e.g., infectious diseases and
	-			entirety. Pancreatic cells that	disorders as described in the
				may be used according to these	"Infectious Diseases" section
				assays are publicly available	below, especially of the
_				(e.g., through the ATCC)	urinary tract and skin), carpal
				and/or may be routinely	tunnel syndrome and
				generated. Exemplary	Dupuytren's contracture).
	_			pancreatic cells that may be	An additional highly preferred
				used according to these assays	indication is obesity and/or
				include rat INS-1 cells. INS-1	complications associated with
				cells are a semi-adherent cell	obesity. Additional highly
				line established from cells	preferred indications include
				isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
				These cells retain	highly preferred indications are
				characteristics typical of native	complications associated with
				pancreatic beta cells including	insulin resistance.
				glucose inducible insulin	
				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:167.	
-	HCE3G69	559	Production of IL-10	Assays for production of IL-10	Highly preferred indications
			and activation of T-	and activation of T-cells are	include allergy and asthma.
			cells.	well known in the art and may	Additional highly preferred
				be used or routinely modified	indications include immune
				to assess the ability of	and hematopoietic disorders

		polypeptides of the invention	(e.g. as described below under
		(including antibodies and	"Immune Activity" and
_		agonists or antagonists of the	"Blood-Related Disorders").
		invention) to stimulate or	autoimmune diseases (e.g.,
		inhibit production of IL-10	rheumatoid arthritis, systemic
		and/or activation of T-cells.	lupus erythematosis, Crohn"s
		Exemplary assays that may be	disease, multiple sclerosis
		used or routinely modified to	and/or as described below),
		assess the ability of	immunodeficiencies (e.g., as
		polypeptides and antibodies of	described below), boosting a T
		the invention (including	cell-mediated immune
		agonists or antagonists of the	response, and suppressing a T
		invention) to modulate IL-10	cell-mediated immune
		production and/or T-cell	response.
		proliferation include, for	
		example, assays such as	
		disclosed and/or cited in:	
		Robinson, DS, et al., "Th-2	
		cytokines in allergic disease"	
		Br Med Bull; 56 (4): 956-968	
		(2000), and Cohn, et al., "T-	
		helper type 2 cell-directed	
		therapy for asthma"	
		Pharmacology & Therapeutics;	
		88: 187-196 (2000); the	
		contents of each of which are	
		herein incorporated by	
		reference in their entirety.	
		Exemplary cells that may be	
		used according to these assays	
		include Th2 cells. IL10	

			-	secreted from Th2 cells may be measured as a marker of Th2	
				cell activation. Th2 cells are	
				a class of T cells that secrete	
				IL4, IL10, IL13, IL5 and IL6.	
				Factors that induce	
				differentiation and activation	
				of Th2 cells play a major role	
				in the initiation and	
				pathogenesis of allergy and	
				asthma. Primary T helper 2	
				cells are generated via in vitro	
				culture under Th2 polarizing	
				conditions using peripheral	
				blood lymphocytes isolated	
				from cord blood.	
HC	HCE5F43	995	Stimulation of	Assays for measuring secretion	A highly preferred
			insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
-			from pancreatic	the art and may be used or	An additional highly preferred
			beta cells.	routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
				Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
				upregulated by glucose and	(e.g., due to diabetic

	also by certain	neilronathy) blood vessel
	proteins/peptides, and	blockage, heart disease, stroke.
	disregulation is a key	impotence (e.g., due to diabetic
	component in diabetes.	neuropathy or blood vessel
	Exemplary assays that may be	blockage), seizures, mental
	used or routinely modified to	confusion, drowsiness,
	test for stimulation of insulin	nonketotic hyperglycemic-
	secretion (from pancreatic	hyperosmolar coma,
	cells) by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Ahren, B., et al.,	diseases and disorders as
	Am J Physiol, 277(4 Pt	described in the
	2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
	al., Endocrinology,	section below), dyslipidemia,
-	138(9):3735-40 (1997); Kim,	endocrine disorders (as
	K.H., et al., FEBS Lett,	described in the "Endocrine
	377(2):237-9 (1995); and,	Disorders" section below),
	Miraglia S et. al., Journal of	neuropathy, vision impairment
	Biomolecular Screening,	(e.g., diabetic retinopathy and
-	4:193-204 (1999), the contents	blindness), ulcers and impaired
-	of each of which is herein	wound healing, and infection
	incorporated by reference in its	(e.g., infectious diseases and
	entirety. Pancreatic cells that	disorders as described in the
	may be used according to these	"Infectious Diseases" section
	assays are publicly available	below, especially of the
	(e.g., through the ATCC)	urinary tract and skin), carpal
	and/or may be routinely	tunnel syndrome and
	generated. Exemplary	Dupuytren's contracture).
	pancreatic cells that may be	An additional highly preferred

			used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992	indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
HCEFB80	561	Activation of transcription through GAS response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkins lymphoma, non-Hodgkins lymphoma, non-Hodgkins lymphoma, non-elanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include

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benign dysproliferative		conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an
routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary mouse T cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary T cells that may be	used according to these assays	include the CTLL cell line,	which is a suspension culture	of IL-2 dependent cytotoxic T	cells.		
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infectious disease as described below under "Infectious Disease"). An additional preferred indication is	idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia,	leukopenia, thrombocytopenia, acute lymphocytic anemia	multiple myeloma, arthritis, AIDS, granulomatous disease,	inflammatory bowel disease, sepsis, neutropenia.	neutrophilia, psoriasis,	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation, diabetes mellitus, endocarditis,	meningitis, Lyme Disease, and asthma and allergy.	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other
										Assays for measuring secretion	of insulin are well-known in	the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	stimulate insulin secretion.
										Insulin Secretion								
										561								
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For example, insulin secretion diseases and disorders as is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel proteins/peptides, and disregulation is a key important in diabetes. Exemplary assays that may be component in diabetes. Exemplary assays that may be component in diabetes. Exemplary assays that may be component in diabetes. Exemplary assays that may be lookage), seizures, mental confusion, drowsiness, nontedion gantibodies of the invention (including antibodies and agonists or antagonists of the invention) include assays and agonists or antagonists of the invention (including antibodies disclosed in: Shimizu, H., et al., Endocr J. 47(3):261-9 (2000), Salapatek, A.M., et al., Biol Chem, 271(28):16544-52 (1998); Olson, L.K., et al., Jesio Chem, 271(28):16544-52 (1996); and, Miraglia S et. al., blindness), ulcers and impaired auti-rat insulain and proteins and infection of insulin antibodies. Biol Chem, 271(28):16544-52 (1996); and, Miraglia S et. al., blindness), ulcers and disorders as dispersional of Biomolecular wound healing. and infection			
For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999),	For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endoor J, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); and, Miraglia S et al., Journal of Biomolecular Screening, 4:193-204 (1999),	For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Mol Endocr J, 47(3):261-9 (2000); Salapatek, A.M., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999),	For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention include assays disclosed in: Shimizu, H., et al., Endocr J, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Pilipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., Jumal of Biomolecular Screening, 4:193-204 (1999),

			reference in its entirety.	"Infectious Diseases" section
		-	Pancreatic cells that may be	below, especially of the
			used according to these assays	urinary tract and skin), carpal
			are publicly available (e.g.,	tunnel syndrome and
			through the ATCC) and/or	Dupuytren's contracture).
			may be routinely generated.	An additional highly preferred
			Exemplary pancreatic cells that	indication is obesity and/or
			may be used according to these	complications associated with
			assays include HITT15 Cells.	obesity. Additional highly
			HITT15 are an adherent	preferred indications include
			epithelial cell line established	weight loss or alternatively,
			from Syrian hamster islet cells	weight gain. Additional highly
			transformed with SV40. These	preferred indications are
			cells express glucagon,	complications associated with
		***	somatostatin, and	insulin resistance.
			glucocorticoid receptors. The	
	_		cells secrete insulin, which is	
			stimulated by glucose and	
	-		glucagon and suppressed by	
			somatostatin or	
			glucocorticoids. ATTC# CRL-	
			1777 Refs: Lord and	
		· ·	Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc.	
			Natl. Acad. Sci. USA 78:	
			4339-4343, 1981.	
HCENK38	562	Protection from	Caspase Apoptosis Rescue.	A highly preferred
		Endothelial Cell	Assays for caspase apoptosis	embodiment of the invention
		Apoptosis.	rescue are well known in the	includes a method for
			art and may be used or	stimulating endothelial cell
			routinely modified to assess	growth. An alternative highly

		the ability of the nolynentides	nreferred embodiment of the
		of the immediate Control	
		of the invention (including	invention includes a method
-		antibodies and agonists or	for inhibiting endothelial cell
		antagonists of the invention) to	growth. A highly preferred
		inhibit caspase protease-	embodiment of the invention
		mediated apoptosis.	includes a method for
		Exemplary assays for caspase	stimulating endothelial cell
		apoptosis that may be used or	proliferation. An alternative
		routinely modified to test	highly preferred embodiment
		caspase apoptosis rescue of	of the invention includes a
-		polypeptides of the invention	method for inhibiting
		(including antibodies and	endothelial cell proliferation.
		agonists or antagonists of the	A highly preferred
	-	invention) include the assays	embodiment of the invention
		disclosed in Romeo et al.,	includes a method for
		Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
		(2000); Messmer et al., Br J	growth. An alternative highly
_		Pharmacol 127(7): 1633-1640	preferred embodiment of the
		(1999); and J Atheroscler	invention includes a method
		Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
		the contents of each of which	growth. A highly preferred
		are herein incorporated by	embodiment of the invention
		reference in its entirety.	includes a method for
		Endothelial cells that may be	stimulating apoptosis of
		used according to these assays	endothelial cells. An
		are publicly available (e.g.,	alternative highly preferred
		through commercial sources).	embodiment of the invention
		Exemplary endothelial cells	includes a method for
		that may be used according to	inhibiting (e.g., decreasing)
		these assays include bovine	apoptosis of endothelial cells.
		aortic endothelial cells	A highly preferred

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embodiment of the invention includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial
(bAEC), which are an example of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.																							
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infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary
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angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud's	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as
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				indications include blood
				disorders (e.g., as described
				below under "Immune
				Activity", "Blood-Related
				Disorders", and/or
				"Cardiovascular Disorders").
				Preferred indications include
				autoimmune diseases (e.g.,
				rheumatoid arthritis, systemic
				lupus erythematosis, multiple
	_			sclerosis and/or as described
				below) and
				immunodeficiencies (e.g., as
				described below). Additional
				preferred indications include
				inflammation and
				inflammatory disorders (such
				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
				and Crohn's disease), and pain
				management.
HCENK38	562	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include neoplastic diseases
		through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
		response element in	Site (GAS) response element	and/or as described below
		immune cells (such	are well-known in the art and	under "Hyperproliferative
		as T-cells).	may be used or routinely	Disorders"). Highly preferred
			modified to assess the ability	indications include neoplasms
			of polypeptides of the	and cancers, such as, for
			invention (including antibodies	example, leukemia, lymphoma

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(, c, T o.11 1	(e.g., 1 cen nymphoma,	Burkitt's lymphoma, non-	Hodgkins lymphoma,	Hodgkin"s disease),	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,
and against or and against of	and agomets of antagomets of	the invention) to regulate	STAT transcription factors and	modulate gene expression	involved in a wide variety of	cell functions. Exemplary	assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary mouse T cells that	may be used according to these
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"Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, arthritis,	AIDS, granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease, and	asthma and allergy.
(e.g., through the ATCC). Exemplary T cells that may be	used according to these assays	which is a suspension culture	of IL-2 dependent cytotoxic T	cells.																								
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	HCFNK38	243	Activotion of	1	
-		700	Activation of	Ninase assay. Ninase assays,	A highly preferred
			Hepatocyte EKK	tor example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating hepatocyte cell
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting
				of polypeptides of the	hepatocyte cell proliferation.
				invention (including antibodies	A highly preferred
				and agonists or antagonists of	embodiment of the invention
				the invention) to promote or	includes a method for
				inhibit cell proliferation,	stimulating hepatocyte cell
				activation, and differentiation.	differentiation. An alternative
				Exemplary assays for ERK	highly preferred embodiment
				kinase activity that may be	of the invention includes a
				used or routinely modified to	method for inhibiting
				test ERK kinase-induced	hepatocyte cell differentiation.
				activity of polypeptides of the	A highly preferred
				invention (including antibodies	embodiment of the invention
				and agonists or antagonists of	includes a method for
				the invention) include the	activating hepatocyte cells. An
				assays disclosed in Forrer et	alternative highly preferred
				al., Biol Chem 379(8-9):1101-	embodiment of the invention
_				1110 (1998); Kyriakis JM,	includes a method for
				Biochem Soc Symp 64:29-48	inhibiting the activation of
				(1999); Chang and Karin,	and/or inactivating hepatocyte
				Nature 410(6824):37-40	cells. Highly preferred
				(2001); and Cobb MH, Prog	indications include disorders of
	-			Biophys Mol Biol 71(3-4):479-	the liver and/or endocrine
				500 (1999); the contents of	disorders (e.g., as described

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below under "Endocrine Disorders"). Preferred indications include neonlastic	diseases (e.g., as described	"Hyperproliferative	Disorders"), blood disorders (e.g., as described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal
each of which are herein incorporated by reference in its entirety. Rat liver hepatoma	cells that may be used	publicly available (e.g.,	unrougn the ATCC). Exemplary rat liver hepatoma	cells that may be used	according to these assays	include H4lle cells, which are	known to respond to	glucocorticoids, insulin, or	cAMP derivatives.																	

Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	helow especially of the

	urinary tract and skin), carpal
	 tunnel syndrome and
	Dupuytren's contracture).
	An additional highly preferred
	indication is obesity and/or
	complications associated with
	obesity. Additional highly
	preferred indications include
	weight loss or alternatively,
	weight gain. Additional
	highly preferred indications are
	complications associated with
	insulin resistance.
	Additional highly preferred
	indications are disorders of the
	musculoskeletal systems
	including myopathies,
	muscular dystrophy, and/or as
	described herein.
	Additional highly preferred
	 indications include, hepatitis,
	jaundice, gallstones, cirrhosis
	of the liver, degenerative or
-	 necrotic liver disease,
	alcoholic liver diseases,
	fibrosis, liver regeneration,
	metabolic disease,
	dyslipidemia and chlolesterol
	metabolism.
	Additional highly preferred
	indications include neoplasms

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					henetoceroinomos other live
					inchatocalonidas, otner niver
		_			cancers, and colon and
					pancreatic cancer. Preferred
					indications also include
					prostate, breast, lung,
					esophageal, stomach, brain,
					and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	HCEWE20	563	Regulation of	Assays for the regulation of	A highly preferred
			transcription of	transcription of Malic Enzyme	indication is diabetes mellitus.
			Malic Enzyme in	are well-known in the art and	An additional highly preferred
			hepatocytes	may be used or routinely	indication is a complication
				modified to assess the ability	associated with diabetes (e.g.,
				of polypeptides of the	diabetic retinopathy, diabetic
				invention (including antibodies	nephropathy, kidney disease
_				and agonists or antagonists of	(e.g., renal failure,
				the invention) to regulate	nephropathy and/or other
				transcription of Malic Enzyme,	diseases and disorders as
				a key enzyme in lipogenesis.	described in the "Renal
				Malic enzyme is involved in	Disorders" section below),
				lipogenesisand its expression is	diabetic neuropathy, nerve
				stimulted by insulin. ME	disease and nerve damage
				promoter contains two direct	(e.g., due to diabetic
				repeat (DR1)- like elements	neuropathy), blood vessel
				MEp and MEd identified as	blockage, heart disease, stroke,

	nutative PPAR response	importance le a due to dishotis
-	Schodest Att 1 Strang	importing (e.g., due to diabetic
	elements. ME promoter may	neuropathy or blood vessel
	also responds to AP1 and other	blockage), seizures, mental
	transcription factors.	confusion, drowsiness,
	Exemplary assays that may be	nonketotic hyperglycemic-
	used or routinely modified to	hyperosmolar coma,
	test for regulation of	cardiovascular disease (e.g.,
	transcription of Malic Enzyme	heart disease, atherosclerosis,
	(in hepatocytes) by	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	disclosed in: Streeper, R.S., et	section below), dyslipidemia,
	al., Mol Endocrinol,	endocrine disorders (as
	12(11):1778-91 (1998);	described in the "Endocrine
	Garcia-Jimenez, C., et al., Mol	Disorders" section below),
	Endocrinol, 8(10):1361-9	neuropathy, vision impairment
	(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
	Biol Chem, 274(25):17997-	blindness), ulcers and impaired
	8004 (1999); Ijpenberg, A., et	wound healing, and infection
	al., J Biol Chem,	(e.g., infectious diseases and
	272(32):20108-20117 (1997);	disorders as described in the
	Berger, et al., Gene 66:1-10	"Infectious Diseases" section
	(1988); and, Cullen, B., et al.,	below, especially of the
	Methods in Enzymol.	urinary tract and skin), carpal
	216:362–368 (1992), the	tunnel syndrome and
	contents of each of which is	Dupuytren's contracture).
	herein incorporated by	An additional highly preferred
	reference in its entirety.	indication is obesity and/or
	Hepatocytes that may be used	complications associated with

according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to these assays includes the mouse assays includes the mouse preadipocyte cell line assays includes the mouse amouse preadipocyte cell line assays includes the mouse and propagate assays includes the mouse associated with assays includes associated with assays includes the mouse associated associated with assays includes the mouse associated with assays includes the	Production of Assays for measuring Preferred embodiments of the invention in the art and may be used or routinely modified to measure ICAM-1 Production of expression of ICAM-1 are invention include using polypeptides of the invention to assess the ability of agonists or antagonists of the invention, and/or treatment of agonists or antagonists of the invention, to regulate ICAM-1 Atherosclerosis, Restenosis, expression. Exemplary assays that may be used or routinely modified to measure ICAM-1
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	HCEWE20

			Atherosclerosis, 149(1):99-110 (2000): Panettieri RA Ir. et al.	
			J Immunol, 154(5):2358-2365	
	-		(1995); and, Grunstein MM, et	
			al., Am J Physiol Lung Cell	
			Mol Physiol, 278(6):L1154-	
			L1163 (2000), the contents of	
			each of which is herein	
			incorporated by reference in its	
			entirety. Cells that may be	
			used according to these assays	
			are publicly available (e.g.,	
			through the ATCC) and/or	
			may be routinely generated.	
			Exemplary cells that may be	
			used according to these assays	
			include Aortic Smooth Muscle	
			Cells (AOSMC); such as	
			bovine AOSMC.	
HCFNN01	564	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as T-cells).	routinely modified to assess	preferred embodiment of the
			the ability of polypeptides of	invention includes a method
			the invention (including	for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate the serum response	indications include blood
			factors and modulate the	disorders (e.g., as described

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below under "Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"), Highly preferred indications	include autoimmune diseases	systemic lupus erythematosis,	Crohn's disease, multiple	sclerosis and/or as described	(e.g., as described below).	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and
expression of genes involved in growth. Exemplary assays for transcription through the	SRE that may be used or routinely modified to test SRE	activity of the polypeptides of	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Derger et al., Gelle 00:1-10 (1998): Cullen and Malm.	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic
	-	_								_															
						-								-											

	activity.	cancers, such as, for example
		lenkemia lymnhoma
		15 diversion 13 mpmonia,
		melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
_		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications include
		anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted
		organs and tissues,
		hemophilia, hypercoagulation,
		diabetes mellitus, endocarditis,
		meningitis, Lyme Disease,

cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	
	Kinase assay: measures the phosphorylation of Elk-1, an indication of activation of extracellular signal regulated kinase (ERK). ERK pathway regulates cell growth, proliferation and differentiation. Cells were pretreated with SID supernatants for 15-18 hours, and then 100 nM of insulin was added to stimulate ERK kinase. Phosphorylation of Elk-1 was measured after a 20 minute incubation. Preacording to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse
	Inhibition of adipocyte ERK signaling pathway.
	565
	HCGMD59

	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel
preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. Cells were differentiated to an adipose-like state before being used in the screen. See Green et al., Cell 3: 127-133 (1974), the contents of which are herein incorporated by reference in its entirety.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain
	Insulin Secretion
	595
	HCGMDS9

	proteins/peptides. and	blockage, heart disease stroke
	disregulation is a key	imnotence (e α due to diahetic
	distribution is a ney	impotence (e.g., and to anabence
	component in diabetes.	neuropathy or blood vessel
	Exemplary assays that may be	blockage), seizures, mental
	used or routinely modified to	confusion, drowsiness,
	test for stimulation of insulin	nonketotic hyperglycemic-
	secretion (from pancreatic	hyperosmolar coma,
	cells) by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Shimizu, H., et	diseases and disorders as
	al., Endocr J, 47(3):261-9	described in the
	(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
	Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
	17 (1999); Filipsson, K., et al.,	endocrine disorders (as
	Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
	(1998); Olson, L.K., et al., J	Disorders" section below),
	Biol Chem, 271(28):16544-52	neuropathy, vision impairment
	(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
	Journal of Biomolecular	blindness), ulcers and impaired
	Screening, 4:193-204 (1999),	wound healing, and infection
-	the contents of each of which	(e.g., infectious diseases and
	is herein incorporated by	disorders as described in the
	reference in its entirety.	"Infectious Diseases" section
	Pancreatic cells that may be	below, especially of the
	used according to these assays	urinary tract and skin), carpal
	are publicly available (e.g.,	tunnel syndrome and
	through the ATCC) and/or	Dupuytren's contracture).
	may be routinely generated.	An additional highly preferred
	Exemplary pancreatic cells that	

	assays include HII 115 Cells.	obesity. Additional highly
	HITTIS are an adherent epithelial cell line established	preferred indications include weight loss or alternatively.
	from Syrian hamster islet cells	weight gain. Additional highly
	transformed with SV40. These	preferred indications are
	cells express glucagon,	complications associated with
	somatostatin, and	insulin resistance.
	glucocorticoid receptors. The	
	cells secrete insulin, which is	
	stimulated by glucose and	
	glucagon and suppressed by	
	somatostatin or	
	glucocorticoids. ATTC# CRL-	
	1777 Refs: Lord and	
	Ashcroft. Biochem. J. 219:	
	547-551; Santerre et al. Proc.	
	Natl. Acad. Sci. USA 78:	
	4339-4343, 1981.	
HCHNF25 566 Calcium flux in	Assays for measuring calcium	Preferred embodiments of the
immune cells (such	flux are well-known in the art	invention include using
as monocytes)	and may be used or routinely	polypeptides of the invention
	modified to assess the ability	(or antibodies, agonists, or
	of polypeptides of the	antagonists thereof) in
	invention (including antibodies	detection, diagnosis,
	and agonists or antagonists of	prevention, and/or treatment of
	the invention) to mobilize	Infection, Inflammation,
	calcium. Cells normally have	Atherosclerosis,
	very low concentrations of	Hypersensitivity, and
	cytosolic calcium compared to	Leukemias
	much higher extracellular	

calcium. Extracellular factors	can cause an influx of calcium,	leading to activation of	calcium responsive signaling	pathways and alterations in	cell functions. Exemplary	assays that may be used or	routinely modified to measure	calcium flux in immune cells	(such as monocytes) include	assays disclosed in: Chan, CC,	et al., J Pharmacol Exp Ther,	269(3):891-896 (1994);	Andersson, K, et al., Cytokine,	12(12):1784-1787 (2000);	Scully, SP, et al., J Clin Invest,	74(2) 589-599 (1984); and,	Sullivan, E, et al., Methods	Mol Biol, 114:125-133 (1999),	the contents of each of which	is herein incorporated by	reference in its entirety. Cells	that may be used according to	these assays are publicly	available (e.g., through the	ATCC) and/or may be	routinely generated.	Exemplary cells that may be	used according to these assays	include the THP-1 monocyte	cell line.
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									-																	•				

HCNDR47	47	567	Regulation of	Assays for the regulation of	A highly preferred indication
			viability and	viability and proliferation of	is diabetes mellitus. An
			proliferation of	cells in vitro are well-known in	additional highly preferred
			pancreatic beta	the art and may be used or	indication is a complication
			cells.	routinely modified to assess	associated with diabetes (e.g.,
				the ability of polypeptides of	diabetic retinopathy, diabetic
				the invention (including	nephropathy, kidney disease
				antibodies and agonists or	(e.g., renal failure,
				antagonists of the invention) to	nephropathy and/or other
				regulate viability and	diseases and disorders as
				proliferation of pancreatic beta	described in the "Renal
				cells. For example, the Cell	Disorders" section below),
				Titer-Glo luminescent cell	diabetic neuropathy, nerve
				viability assay measures the	disease and nerve damage
				number of viable cells in	(e.g., due to diabetic
				culture based on quantitation	neuropathy), blood vessel
				of the ATP present which	blockage, heart disease, stroke,
				signals the presence of	impotence (e.g., due to diabetic
				metabolically active cells.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
	•			test regulation of viability and	nonketotic hyperglycemic-
				proliferation of pancreatic beta	hyperosmolar coma,
				cells by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,
				the invention) include assays	hypertension, stroke, and other
_				disclosed in: Friedrichsen BN,	diseases and disorders as
				et al., Mol Endocrinol,	described in the
				15(1):136-48 (2001); Huotari	"Cardiovascular Disorders"
				MA, et al., Endocrinology,	section below), dyslipidemia,

				139(4):1494-9 (1998): Hugl	endocrine disorders (as
_				SR. et al J Biol Chem 1998	described in the "Endocrine
				Jul 10;273(28):17771-9	Disorders" section below),
				(1998), the contents of each of	neuropathy, vision impairment
				which is herein incorporated	(e.g., diabetic retinopathy and
				by reference in its entirety.	blindness), ulcers and impaired
				Pancreatic cells that may be	wound healing, and infection
				used according to these assays	(e.g., infectious diseases and
_				are publicly available (e.g.,	disorders as described in the
				through the ATCC) and/or	"Infectious Diseases" section
				may be routinely generated.	below, especially of the
				Exemplary pancreatic cells that	urinary tract and skin), carpal
				may be used according to these	tunnel syndrome and
				assays include rat INS-1 cells.	Dupuytren's contracture). An
				INS-1 cells are a semi-	additional highly preferred
-				adherent cell line established	indication is obesity and/or
	-			from cells isolated from an X-	complications associated with
				ray induced rat transplantable	obesity. Additional highly
				insulinoma. These cells retain	preferred indications include
				characteristics typical of native	weight loss or alternatively,
				pancreatic beta cells including	weight gain. Additional highly
				glucose inducible insulin	preferred indications are
				secretion. References: Asfari	complications associated with
				et al. Endocrinology 1992	insulin resistance.
	HCNDR47	295	Production of	RANTES FMAT Assays for	
			RANTES in	immunomodulatory proteins	
			endothelial cells	that induce chemotaxis of T	
			(such as human	cells, monocytes, and	
			umbilical vein	eosinophils are well known in	
			endothelial cells	the art and may be used or	

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routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	induce chemotaxis, and/or	mediate humoral or cell-	mediated immunity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as RANTES,	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp
(HUVEC))																								711.0						

			Immunol 101(3):398-407	
			(1995), the contents of each of	
			which are herein incorporated	
			by reference in its entirety.	
			Endothelial cells that may be	
			used according to these assays	
			are publicly available (e.g.,	
			through the ATCC).	
			Exemplary endothelial cells	
			that may be used according to	
			these assays include human	
			umbilical vein endothelial cells	
			(HUVEC), which are	
			endothelial cells which line	
			venous blood vessels, and are	
			involved in functions that	
			include, but are not limited to,	
			angiogenesis, vascular	
			permeability, vascular tone,	
			and immune cell extravasation.	
HCNSB61	268	Activation of	Kinase assay. Kinase assays,	A highly preferred
		Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
	-	Signaling Pathway	assay, for ERK signal	includes a method for
			transduction that regulate cell	stimulating adipocyte
			proliferation or differentiation	proliferation. An alternative
			are well known in the art and	highly preferred embodiment
			may be used or routinely	of the invention includes a
			modified to assess the ability	method for inhibiting
			of polypeptides of the	adipocyte proliferation. A
			invention (including antibodies	highly preferred embodiment
			and agonists or antagonists of	of the invention includes a

method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention	includes a method for includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method	for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment	of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adinocytes	Highly preferred indications include endocrine disorders (e.g., as described below under	"Endocrine Disorders"). Highly preferred indications also include neoplastic diseases (e.g., lipomas,	liposarcomas, and/or as described below under "Hyperproliferative Disorders") Preferred	indications include blood disorders (e.g., hypertension, congestive heart failure, blood
the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for FRK	kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999);	Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature	410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which	are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these	assays are publicly available (e.g., through the ATCC).

		cells that may be used	vessel blockage, heart disease,
		according to these assays	stroke, impotence and/or as
		include 3T3-L1 cells. 3T3-L1	described below under
		is an adherent mouse	"Immune Activity",
		preadipocyte cell line that is a	"Cardiovascular Disorders",
		continuous substrain of 3T3	and/or "Blood-Related
		fibroblast cells developed	Disorders"), immune disorders
		through clonal isolation and	(e.g., as described below under
		undergo a pre-adipocyte to	"Immune Activity"), neural
		adipose-like conversion under	disorders (e.g., as described
		appropriate differentiation	below under "Neural Activity
		conditions known in the art.	and Neurological Diseases"),
			and infection (e.g., as
			described below under
			"Infectious Disease").
			A highly preferred indication
			is diabetes mellitus. An
_			additional highly preferred
			indication is a complication
			associated with diabetes (e.g.,
			diabetic retinopathy, diabetic
			nephropathy, kidney disease
			(e.g., renal failure,
			nephropathy and/or other
			diseases and disorders as
			described in the "Renal
			Disorders" section below),
			diabetic neuropathy, nerve
	•		disease and nerve damage
			(e.g., due to diabetic
			neuropathy), blood vessel

		d ii.	blockage, heart disease, stroke, impotence (e.g., due to diabetic
		<u> </u>	neuropathy or blood vessel blockage), seizures, mental
		3 6	confusion, drowsiness,
		<u> </u>	hyperosmolar coma,
-	-	3	cardiovascular disease (e.g.,
		<u>h</u>	heart disease, atherosclerosis,
	-	<u>u</u>	microvascular disease,
			hypertension, stroke, and other
		р	diseases and disorders as
		Þ	described in the
			"Cardiovascular Disorders"
		<u>ж</u>	section below), dyslipidemia,
	-	Б <u>-</u>	endocrine disorders (as
		יס 	described in the "Endocrine
		<u>Ω</u>	Disorders" section below),
		ū	neuropathy, vision impairment
		9)	(e.g., diabetic retinopathy and
		q	blindness), ulcers and impaired
		8	wound healing, infection (e.g.,
		-ii	infectious diseases and
		<u> </u>	disorders as described in the
			"Infectious Diseases" section
		<u> </u>	below (particularly of the
		in	urinary tract and skin). An
		- 8	additional highly preferred
		ir	indication is obesity and/or
		<u> </u>	complications associated with
		0	obesity. Additional highly

preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	lymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred	indications include melanoma,	prostate, lung, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer.	Highly preferred indications
				,											-															
		-11						-							-															
								-											-											

				include lipomas and
				liposarcomas. Other preferred
				indications include benign
				dysproliferative disorders and
				pre-neoplastic conditions, such
				as, for example, hyperplasia,
				metaplasia, and/or dysplasia.
HCNSB61	268	Endothelial Cell	Caspase Apoptosis. Assays for	A highly preferred
		Apoptosis	caspase apoptosis are well	embodiment of the invention
			known in the art and may be	includes a method for
			used or routinely modified to	stimulating endothelial cell
-			assess the ability of	growth. An alternative highly
-			polypeptides of the invention	preferred embodiment of the
			(including antibodies and	invention includes a method
-			agonists or antagonists of the	for inhibiting endothelial cell
			invention) to promote caspase	growth. A highly preferred
			protease-mediated apoptosis.	embodiment of the invention
			Induction of apoptosis in	includes a method for
			endothelial cells supporting the	stimulating endothelial cell
			vasculature of tumors is	proliferation. An alternative
			associated with tumor	highly preferred embodiment
			regression due to loss of tumor	of the invention includes a
			blood supply. Exemplary	method for inhibiting
			assays for caspase apoptosis	endothelial cell proliferation.
			that may be used or routinely	A highly preferred
			modified to test capase	embodiment of the invention
			apoptosis activity of	includes a method for
			polypeptides of the invention	stimulating apoptosis of
			(including antibodies and	endothelial cells. An
			agonists or antagonists of the	alternative highly preferred
			invention) include the assays	embodiment of the invention

includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfinction atherosclerosis
disclosed in Lee et al., FEBS	Lett 485(2-3): 122-126 (2000);	Nor et al., J Vasc Res 37(3):	209-218 (2000); and Karsan	and Harlan, J Atheroscler	Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through commercial sources).	Exemplary endothelial cells	that may be used according to	these assays include bovine	aortic endothelial cells	(bAEC), which are an example	of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.						
																							_							
														_										-	_	-				
						-																		<u>-</u>		_		-		

		and atherosclerotic vascular
		disease, diabetic nephropathy,
	-	intracardiac shunt, cardiac
		hypertrophy, myocardial
		infarction, chronic
		hemodynamic overload, and/or
		 as described below under
		 "Cardiovascular Disorders").
		Highly preferred indications
		 include cardiovascular,
		endothelial and/or angiogenic
		disorders (e.g., systemic
		 disorders that affect vessels
		such as diabetes mellitus, as
	_	well as diseases of the vessels
		 themselves, such as of the
		arteries, capillaries, veins
		and/or lymphatics). Highly
		preferred are indications that
		stimulate angiogenesis and/or
		cardiovascularization. Highly
		 preferred are indications that
		inhibit angiogenesis and/or
		 cardiovascularization.
		Highly preferred indications
		 include antiangiogenic activity
		to treat solid tumors,
		leukemias, and Kaposi"s
		 sarcoma, and retinal disorders.
-		Highly preferred indications
		include neoplasms and cancer,

such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, hacillary	angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred	indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as atheresclerosis	hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as

thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred
																					-									
													-				-													

					indications include fibromas.
					heart disease, cardiac arrest,
					heart valve disease, and
					vascular disease.
٠					Preferred indications include
					blood disorders (e.g., as
					described below under
			-	-	"Immune Activity", "Blood-
		-			Related Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
`					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
			-		inflammation and
	,				inflammatory disorders (such
					as acute and chronic
	-				inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
	21011011				management.
	HCNSM70	569	Myoblast cell	Assays for muscle cell	Highly preferred indications
			proliferation	proliferation are well known in	include diabetes, myopathy,
				the art and may be used or	muscle cell atrophy, cancers of
	70			routinely modified to assess	muscle (such as,
				the ability of polypeptides of	rhabdomyoma, and

			-																									
rhabdosarcoma), cardiovascular disorders (such	as congestive heart failure,	congenital cardiovascular	abnormalities, heart disease,	cardiac arrest, heart valve	disease, vascular disease, and	also as described below under	"Cardiovascular Disorders"),	stimulating myoblast	proliferation, and inhibiting	myoblast proliferation.																		
the invention (including antibodies and agonists or	antagonists of the invention) to stimulate or inhihit myohlast	cell proliferation. Exemplary	assays for myoblast cell	proliferation that may be used	or routinely modified to test	activity of polypeptides and	antibodies of the invention	(including agonists or	antagonists of the invention)	include, for example, assays	disclosed in: Soeta, C., et al.	"Possible role for the c-ski	gene in the proliferation of	myogenic cells in regenerating	skeletal muscles of rats" Dev	Growth Differ Apr;43(2):155-	64 (2001); Ewton DZ, et al.,	"IGF binding proteins-4, -5	and -6 may play specialized	roles during L6 myoblast	proliferation and	differentiation" J Endocrinol	Mar;144(3):539-53 (1995);	and, Pampusch MS, et	al.,"Effect of transforming	growth factor beta on	proliferation of L6 and	embryonic porcine myogenic
																-					-							

			cells" J Cell Physiol Jun;143(3):524-8 (1990); the contents of each of which are herein incorporated by	
			reference in their entirety. Exemplary myoblast cells that may be used according to these	
			assays include the rat myoblast L6 cell line. Rat myoblast L6	
			cells are an adherent rat myoblast cell line, isolated	
			from primary cultures of rat	
			ningn muscie, that fuse to form multinucleated myotubes and	
			striated fibers after culture in	
1101101744	000		differentiation media.	
HCUCK44	2/0	Protection from	Caspase Apoptosis Rescue.	A highly preferred
		Endothelial Cell	Assays for caspase apoptosis	embodiment of the invention
		Apoptosis.	rescue are well known in the	includes a method for
			art and may be used or	stimulating endothelial cell
			routinely modified to assess	growth. An alternative highly
			the ability of the polypeptides	preferred embodiment of the
			of the invention (including	invention includes a method
			antibodies and agonists or	for inhibiting endothelial cell
			antagonists of the invention) to	growth. A highly preferred
			inhibit caspase protease-	embodiment of the invention
			mediated apoptosis.	includes a method for
			Exemplary assays for caspase	stimulating endothelial cell
			apoptosis that may be used or	proliferation. An alternative
			routinely modified to test	highly preferred embodiment
			caspase apoptosis rescue of	of the invention includes a

4 - 0 - 0 - 0 - 0 - 0 - 0 - 0 - 0 - 0 -		polypeptides of the invention	method for inhibiting
		(including antibodies and	endothelial cell proliferation.
		agonists or antagonists of the	A highly preferred
		invention) include the assays	embodiment of the invention
		disclosed in Romeo et al.,	includes a method for
	-	Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
		(2000); Messmer et al., Br J	growth. An alternative highly
		Pharmacol 127(7): 1633-1640	preferred embodiment of the
		(1999); and J Atheroscler	invention includes a method
		Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
		the contents of each of which	growth. A highly preferred
		are herein incorporated by	embodiment of the invention
		reference in its entirety.	includes a method for
		Endothelial cells that may be	stimulating apoptosis of
		used according to these assays	endothelial cells. An
		are publicly available (e.g.,	alternative highly preferred
		through commercial sources).	embodiment of the invention
		Exemplary endothelial cells	includes a method for
		that may be used according to	inhibiting (e.g., decreasing)
		these assays include bovine	apoptosis of endothelial cells.
		aortic endothelial cells	A highly preferred
-		(bAEC), which are an example	embodiment of the invention
		of endothelial cells which line	includes a method for
		blood vessels and are involved	stimulating angiogenisis. An
		in functions that include, but	alternative highly preferred
		are not limited to,	embodiment of the invention
		angiogenesis, vascular	includes a method for
		permeability, vascular tone,	inhibiting angiogenesis. A
Of the in		and immune cell extravasation.	highly preferred embodiment
			of the invention includes a
method f			method for reducing cardiac

hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders").
Highly preferred indications include cardiovascular.
endothelial and/or angiogenic
disorders (e.g., systemic
 disorders that affect vessels

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well as diseases of the vessels themselves, such as of the arteries canillaries veins	and/or lymphatics). Highly preferred are indications that	stimulate angiogenesis and/or cardiovascularization. Highly	preferred are indications that	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal.
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stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,
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cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph
angrogenests, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest,
heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic limits of the cardiovascular diseases (e.g., rheumatoid arthritis, systemic limits of the cardiovascular diseases (e.g., rheumatoid arthritis, systemic limits of the cardiovascular diseases (e.g., rheumatoid arthritis, systemic limits of the cardiovascular diseases (e.g., rheumatoid arthritis, systemic limits of the cardiovascular diseases (e.g., rheumatoid arthritis, systemic limits of the cardiovascular diseases (e.g., rheumatoid arthritis, systemic limits of the cardiovascular diseases (e.g., rheumatoid arthritis, systemic limits of the cardiovascular diseases (e.g., rheumatoid arthritis, systemic limits of the cardiovascular diseases (e.g., rheumatoid arthritis).

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	Surface manches, such as		blood disorders (e.g., as
	monocyte chemoattractant		described below under
	protein (MCP), and the	9	"Immune Activity", "Blood-
	activation of monocytes and T		Related Disorders", and/or
	cells. Such assays that may be		"Cardiovascular Disorders").
	used or routinely modified to		Highly preferred indications
	test immunomodulatory and		include autoimmune diseases
	diffferentiation activity of		(e.g., rheumatoid arthritis,
	polypeptides of the invention	-	systemic lupus erythematosis,
	(including antibodies and		multiple sclerosis and/or as
-	agonists or antagonists of the		described below) and
	invention) include assays		immunodeficiencies (e.g., as
	disclosed in Miraglia et al., J		described below). Preferred
	Biomolecular Screening 4:193-	-	indications also include
	204(1999); Rowland et al.,		anemia, pancytopenia,
	"Lymphocytes: a practical		leukopenia, thrombocytopenia,
	approach" Chapter 6:138-160		Hodgkin's disease, acute
	(2000); Satthaporn and		lymphocytic anemia (ALL),
	Eremin, J R Coll Surg Ednb	3dnb	plasmacytomas, multiple
-	45(1):9-19 (2001); and		myeloma, Burkitt's lymphoma,
	Verhasselt et al., J Immunol		arthritis, AIDS, granulomatous
	158:2919-2925 (1997), the		disease, inflammatory bowel
	contents of each of which are		disease, sepsis, neutropenia,
	herein incorporated by		neutrophilia, psoriasis,
	reference in its entirety.		suppression of immune
	Human dendritic cells that may		reactions to transplanted
	be used according to these		organs and tissues,
	assays may be isolated using		hemophilia, hypercoagulation,
	techniques disclosed herein or		diabetes mellitus, endocarditis,
	otherwise known in the art.	-	meningitis (bacterial and
	Human dendritic cells are		viral), Lyme Disease, asthma.

				antigen presenting cells in suspension culture. which	and allergy Preferred indications also include
				when activated by antigen	neoplastic diseases (e.g.,
_				and/or cytokines, initiate and	leukemia, lymphoma, and/or as
				upregulate T cell proliferation	described below under
				and functional activities.	"Hyperproliferative
					Disorders"). Highly preferred
					indications include neoplasms
					and cancers, such as, leukemia,
			-	•	lymphoma, prostate, breast,
					lung, colon, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
	0,001,101				metaplasia, and/or dysplasia.
	HCUECOO	5/1	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
		,	immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
_				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described

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below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and
expression of genes involved	in growth and upregulate the	function of growth-related	genes in many cell types.	Exemplary assays for	transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line.
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cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g.,	malignant glioma), solid tumors, and prostate, breast,	lung, colon, pancreatic, esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,
which is a human natural killer cell line with cytolytic and cytotoxic activity.							-					•												-
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		-			cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HCUHK65	572	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
-				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
-				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
	-			transcription through the SRE	include autoimmune diseases
-				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn's disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
-		-		the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated

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immune response, and suppressing a T cell-mediated immune response. Additional	highly preferred indications include inflammation and	inflammatory disorders, and	treating joint damage in patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,
66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	38/3 (1994); and Black et al., Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.										
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				metaplasia, and/or dvsplasia.
 				Preferred indications include
				anemia, pancytopenia,
				leukopenia, thrombocytopenia,
				Hodgkin's disease, acute
				lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS, granulomatous
				disease, inflammatory bowel
	-			disease, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues, hemophilia,
				hypercoagulation, diabetes
				mellitus, endocarditis,
				meningitis, Lyme Disease,
				cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication
				is infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
HCUIW65	573	Regulation of	Assays for the regulation of	A highly preferred indication
		transcription via	transcription through the	is diabetes mellitus.
		DMEF1 response	DMEF1 response element are	Additional highly preferred
		element in	well-known in the art and may	indications include
		adipocytes and pre-	be used or routinely modified	complications associated with
		adipocytes	to assess the ability of	diabetes (e.g., diabetic
			polypeptides of the invention	retinopathy, diabetic

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lisease		ther	s as	al	low),	erve	lage)	ssel	e, stro	o diabe	essel	ental	٠.٠	mic-		; (e.g.,	lerosis	•	and oth	as		'ders"	idemia	တ	crine	ow),	bairme	thy and
dney c	ıre,	d/or ot	orders	"Reng	on bel	athy, n	ve dan	betic	od ve	diseas	, due to	lood v	ıres, m	siness	rglyce	oma,	lisease	herosc	isease	roke, a	orders		Disor	dyslipi	lers (a	"Endo	on belo	on im	tinopa
thy, ki	al failt	thy an	and dis	in the	s" secti	europ	nd ner	to dia	ıy), ble	, heart	e (e.g.,	y or b	, seizu	ı, drow	c hype	olar co	cular c	ase, at	cular d	ion, st	ınd dis	in the	scular	·low),	disorc	in the	" secti	ıy, visi	etic re
nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and
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pui	of the	he	nent in	h as th		ate	he	ent is		MEF2	i anoth	t is	gulation	skeleta	prima	sose	nuscle	ys that	ly	(EF1	ity (in	pocyte		tibodi	ists of	assays	, et al.,	285-92	(1998); Mora, S., et al., J Biol
odies a	gonists	tivate t	se elen	ct (sac	LUT4	o regul	on. T	se elen	LUT4	nds to	tor and	tor tha	ılin reg	ion in	t is the	ve gluc	t and n	ry assa	outine	for DN	ıt activ	re-adi	of the	ling ar	ıntagoı	clude a	, M.V.	23):14	, et al.
g antib	or anta) to ac	espon:	onstru	g the (and to	oducti	espon:	the G	and bi	ion fac	ion fac	or insu	xpress	3LUT	sponsi	r in fa	empla	sed or 1	to test	elemer	s and p	ptides	(inclu	sts or a	ion) in	inThai	n, 273(ora, S.
(including antibodies and	agonists or antagonists of the	invention) to activate the	DMEF1 response element in a	reporter construct (such as that	containing the GLUT4	promoter) and to regulate	insulin production. The	DMEF1 response element is	present in the GLUT4	promoter and binds to MEF2	transcription factor and another	transcription factor that is	required for insulin regulation	of Glut4 expression in skeletal	muscle. GLUT4 is the primary	insulin-responsive glucose	transporter in fat and muscle	tissue. Exemplary assays that	may be used or routinely	modified to test for DMEF1	response element activity (in	adipocytes and pre-adipocytes)	by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Thai, M.V., et al., J	Biol Chem, 273(23):14285-92	98); M
<u></u>	289	. <u>E</u>	ā	ref	<u> </u>	pro	ins		pre	- pr	tra	tra	red	Jo	nm	ins	tra	tiss	ma	<u> </u>	res	adi	þ	inv	anc	the	dis	Bic	(19
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				undergo a pre-adinocyte to	
				adipose-like conversion under	
				appropriate differentiation culture conditions.	
	HCUIM65	573	Activation of	Assays for the activation of	A highly preferred indication
			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
		_	response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
				invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
			,	factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
				functions. For example, a	nephropathy and/or other
				3T3-L1/CRE reporter assay	diseases and disorders as
				may be used to identify factors	described in the "Renal
				that activate the cAMP	Disorders" section below),
				signaling pathway. CREB	diabetic neuropathy, nerve
				plays a major role in	disease and nerve damage
				adipogenesis, and is involved	(e.g., due to diabetic
				in differentiation into	neuropathy), blood vessel
				adipocytes. CRE contains the	blockage, heart disease, stroke,
				binding sequence for the	impotence (e.g., due to diabetic
_				transcription factor CREB	neuropathy or blood vessel
				(CRE binding protein).	blockage), seizures, mental
				Exemplary assays for	confusion, drowsiness,

	transcription through the	nonketotic hynerolycemic-
	cAMP response element that	hyperosmolar coma,
	may be used or routinely	cardiovascular disease (e.g.,
	modified to test cAMP-	heart disease, atherosclerosis,
	response element activity of	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	disclosed in Berger et al., Gene	section below), dyslipidemia,
	66:1-10 (1998); Cullen and	endocrine disorders (as
	Malm, Methods in Enzymol	described in the "Endocrine
-	216:362-368 (1992); Henthorn	Disorders" section below),
	et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
	85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
	et al., Mol Cell Biol	blindness), ulcers and impaired
	20(3):1008-1020 (2000); and	wound healing, and infection
	Klemm et al., J Biol Chem	(e.g., infectious diseases and
	273:917-923 (1998), the	disorders as described in the
	contents of each of which are	"Infectious Diseases" section
	herein incorporated by	below, especially of the
	reference in its entirety. Pre-	urinary tract and skin), carpal
	adipocytes that may be used	tunnel syndrome and
	according to these assays are	Dupuytren's contracture).
	publicly available (e.g.,	Additional highly preferred
-	through the ATCC) and/or	indications are complications
	may be routinely generated.	associated with insulin
	Exemplary mouse adipocyte	resistance.
	cells that may be used	
	according to these assays	
	include 3T3-L1 cells. 3T3-L1	

	indication sesity. referred weight loss ight gain. y preferred es mellitus. y preferred plication betes (e.g., ', diabetic y disease other ers as enal ocher ers as enal	vesse]
	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic	neuropathy), blood vessel
is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention)	include assays disclosed in
	Activation of transcription through serum response element in pre-adipocytes.	
	573	
	HCUIM65	

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hloologo boom discons	Ulochage, liealt disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness.	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below). Additional highly	preferred indications are	complications associated with	insulin resistance.		
Berger et al Gene 66:1-10	(1000), O. 11	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. Pre-	adipocytes that may be used	according to these assays are	publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.	Reporter Assay: construct	contains regulatory and coding
	-									-																				Inhibition of	squalene synthetase
																														573	
																														HCUIM65	
								_										_													

			gene transcription.	sequence of squalene	
				synthetase, the first specific	
				enzyme in the cholesterol	
				biosynthetic pathway. See	
				Jiang, et al., J. Biol. Chem.	
				268:12818-128241(993), the	
		_		contents of which are herein	
				incorporated by reference in its	
				entirety. Cells were treated	
				with SID supernatants, and	
				SEAP activity was measured	
				after 72 hours. HepG2 is a	
				human hepatocellular	
				carcinoma cell line (ATCC	
		•		HB-8065). See Knowles et al.,	
			-	Science. 209:497-9 (1980), the	
				contents of which are herein	
				incorporated by reference in its	
				entirety.	
H	HCUIM65	573	Stimulation of	Assays for measuring calcium	A highly preferred
			Calcium Flux in	flux are well-known in the art	indication is diabetes mellitus.
•			pancreatic beta	and may be used or routinely	An additional highly preferred
			cells.	modified to assess the ability	indication is a complication
				of polypeptides of the	associated with diabetes (e.g.,
	5,41			invention (including antibodies	diabetic retinopathy, diabetic
				and agonists or antagonists of	nephropathy, kidney disease
	_			the invention) to mobilize	(e.g., renal failure,
		_		calcium. For example, the	nephropathy and/or other
				FLPR assay may be used to	diseases and disorders as
				measure influx of calcium.	described in the "Renal
				Cells normally have very low	Disorders" section below),

	concentrations of cytosolic	diahetic neuronathy neme
		diacette incui opanity, inci ve
	calcium compared to much	disease and nerve damage
	higher extracellular calcium.	(e.g., due to diabetic
	Extracellular factors can cause	neuropathy), blood vessel
	an influx of calcium, leading to	blockage, heart disease, stroke,
	activation of calcium	impotence (e.g., due to diabetic
	responsive signaling pathways	neuropathy or blood vessel
	and alterations in cell	blockage), seizures, mental
	functions. Exemplary assays	confusion, drowsiness,
	that may be used or routinely	nonketotic hyperglycemic-
	modified to measure calcium	hyperosmolar coma,
	flux by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Satin LS, et al.,	diseases and disorders as
	Endocrinology, 136(10):4589-	described in the
	601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
	Endocrinology, 136(7):2960-6	section below), dyslipidemia,
	(1995); Richardson SB, et al.,	endocrine disorders (as
-	Biochem J, 288 (Pt 3):847-51	described in the "Endocrine
	(1992); and, Meats, JE, et al.,	Disorders" section below),
	Cell Calcium 1989 Nov-	neuropathy, vision impairment
	Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
	contents of each of which is	blindness), ulcers and impaired
	herein incorporated by	wound healing, and infection
	reference in its entirety.	(e.g., infectious diseases and
	Pancreatic cells that may be	disorders as described in the
	used according to these assays	"Infectious Diseases" section
	are publicly available (e.g.,	below, especially of the
	through the ATCC) and/or	urinary tract and skin), carpal

				may be routinely generated.	tunnel syndrome and
				Exemplary pancreatic cells that	Dupuytren's contracture).
				may be used according to these	An additional highly preferred
				assays include HITT15 Cells.	indication is obesity and/or
				HITT15 are an adherent	complications associated with
				epithelial cell line established	obesity. Additional highly
				from Syrian hamster islet cells	preferred indications include
				transformed with SV40. These	weight loss or alternatively,
				cells express glucagon,	weight gain. Aditional
				somatostatin, and	highly preferred indications are
				glucocorticoid receptors. The	complications associated with
				cells secrete insulin, which is	insulin resistance.
				stimulated by glucose and	
		-		glucagon and suppressed by	
				somatostatin or	
-				glucocorticoids. ATTC# CRL-	
				1777 Refs: Lord and	
				Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc.	
				Natl. Acad. Sci. USA 78:	
				4339-4343, 1981.	
	HCUIM65	573	Activation of	This reporter assay measures	Highly preferred indications
			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
	,			cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also

		art and may be used or	as described below under
		routinely modified to assess	"Immune Activity", "Blood-
		the ability of polypeptides of	Related Disorders", and/or
		the invention (including	"Cardiovascular Disorders").
_		antibodies and agonists or	Preferred indications include
		antagonists of the invention) to	autoimmune diseases (e.g.,
		regulate GATA3 transcription	rheumatoid arthritis, systemic
		factors and modulate	lupus erythematosis, multiple
	-	expression of mast cell genes	sclerosis and/or as described
		important for immune response	below) and
-		development. Exemplary	immunodeficiencies (e.g., as
		assays for transcription	described below). Preferred
		through the GATA3 response	indications include neoplastic
		element that may be used or	diseases (e.g., leukemia,
		routinely modified to test	lymphoma, melanoma,
		GATA3-response element	prostate, breast, lung, colon,
		activity of polypeptides of the	pancreatic, esophageal,
		invention (including antibodies	stomach, brain, liver, and
		and agonists or antagonists of	urinary tract cancers and/or as
		the invention) include assays	described below under
		disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Malm, Methods in Enzymol	indications include benign
		216:362-368 (1992); Henthorn	dysproliferative disorders and
		et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
		85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
		et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
		Quant Biol 64:563-571 (1999);	Preferred indications include
		Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
		J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,

				(1999); Zheng and Flavell,	leukemias. Hodgkin's disease.
				Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
				Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
				14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
_				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
	_			Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
		-		these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HCUIW65	573	Activation of	This reporter assay measures	Highly preferred indications
			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also

	Activated T cells (NFAT)	include blood disorders (e.g.,
	response element are well-	as described below under
	known in the art and may be	"Immune Activity", "Blood-
	used or routinely modified to	Related Disorders", and/or
	assess the ability of	"Cardiovascular Disorders").
-	polypeptides of the invention	Preferred indications include
	(including antibodies and	autoimmune diseases (e.g.,
	agonists or antagonists of the	rheumatoid arthritis, systemic
	invention) to regulate NFAT	lupus erythematosis, multiple
	transcription factors and	sclerosis and/or as described
	modulate expression of genes	below) and
	involved in	immunodeficiencies (e.g., as
	immunomodulatory functions.	described below). Preferred
	Exemplary assays for	indications include neoplastic
	transcription through the	diseases (e.g., leukemia,
	NFAT response element that	lymphoma, melanoma,
	may be used or routinely	prostate, breast, lung, colon,
	modified to test NFAT-	pancreatic, esophageal,
	response element activity of	stomach, brain, liver, and
	polypeptides of the invention	urinary tract cancers and/or as
	(including antibodies and	described below under
-	agonists or antagonists of the	"Hyperproliferative
	invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include
	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,

				et al., J Immunol	leukemias, Hodgkin's disease.
				165(12):7215-7223 (2000);	acute lymphocytic anemia
				Hutchinson and McCloskey, J	(ALL), plasmacytomas,
_				Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
				16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
				al., J Exp Med 188:527-537	granulomatous disease,
				(1998), the contents of each of	inflammatory bowel disease,
_				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
	_			publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
				Exemplary human mast cells	mellitus, endocarditis,
			-	that may be used according to	meningitis, and Lyme Disease.
				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
-				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HCUIW65	573	Activation of	This reporter assay measures	Highly preferred indication
			transcription	activation of the NFkB	includes allergy, asthma, and
			through NFKB	signaling pathway in HMC-1	rhinitis. Additional highly
			response element in	human mast cell line.	preferred indications include
			immune cells (such	Activation of NFkB in mast	infection (e.g., an infectious
			as mast cells).	cells has been linked to	disease as described below
				production of certain	under "Infectious Disease"),
				cytokines, such as IL-6 and IL-	and inflammation and

					_		_	-																						
inflammatory disorders.	Preferred indications include	immunological and	hempatopoietic disorders (e.g.,	as described below under	William ("Immune Activity", and	with "Blood-Related Disorders").	Preferred indications also	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications also include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancer, such as, for	example, leukemia, lymphoma,	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary tract cancers and	as described below under	"III"
9. Assays for the activation of	transcription through the	NFKB response element are	well-known in the art and may	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Stassen	et al, J Immunol 166(7):4391-8	(1001). and Managed and
																	_								_					
											_	_																	-	

				Walker, J Allergy Clin	Disorders".
-				Immunol 105(3):500-5 (2000),	
		-		the contents of each of which	
				are herein incorporated by	
				reference in its entirety. Mast	
				cells that may be used	
				according to these assays are	
				publicly available (e.g.,	
				through the ATCC).	
		-		Exemplary human mast cells	
				that may be used according to	
				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HCUIW65	573	Production of	Assays for measuring	Highly preferred indications
	-		VCAM in	expression of VCAM are well-	include inflammation (acute
			endothelial cells	known in the art and may be	and chronic), restnosis,
			(such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred
			endothelial cells	polypeptides of the invention	indications include
			(HUVEC))	(including antibodies and	inflammation and
				agonists or antagonists of the	inflammatory disorders,
				invention) to regulate VCAM	immunological disorders,
				expression. For example,	neoplastic disorders (e.g.
				FMAT may be used to meaure	cancer/tumorigenesis), and
				the upregulation of cell surface	cardiovascular disorders (such

			VCAM-1 expression in	as described below under
			endothelial cells. Endothelial	"Immune Activity". "Blood-
			cells are cells that line blood	Related Disorders",
			vessels, and are involved in	"Hyperproliferative Disorders"
			functions that include, but are	and/or "Cardiovascular
 			not limited to, angiogenesis,	Disorders"). Highly preferred
			vascular permeability, vascular	indications include neoplasms
 			tone, and immune cell	and cancers such as, for
			extravasation. Exemplary	example, leukemia, lymphoma,
			endothelial cells that may be	melanoma, renal cell
			used according to these assays	carcinoma, and prostate,
			include human umbilical vein	breast, lung, colon, pancreatic,
			endothelial cells (HUVEC),	esophageal, stomach, brain,
			which are available from	liver and urinary cancer. Other
			commercial sources. The	preferred indications include
			expression of VCAM	benign dysproliferative
			(CD106), a membrane-	disorders and pre-neoplastic
			associated protein, can be	conditions, such as, for
			upregulated by cytokines or	example, hyperplasia,
 			other factors, and contributes	metaplasia, and/or dysplasia.
			to the extravasation of	•
			lymphocytes, leucocytes and	
			other immune cells from blood	
			vessels; thus VCAM	
			expression plays a role in	
			promoting immune and	
			inflammatory responses.	
HCUIW65	573	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include blood disorders (e.g.,
		through NFAT	Nuclear Factor of Activated T	as described below under
		response element in	cells (NFAT) response element	"Immune Activity", "Blood-

immune cells (such	are well-known in the art and	Related Disorders" and/or
as natural killer	may be used or routinely	"Cardiovascular Disorders").
cells).	modified to assess the ability	Highly preferred indications
	of polypeptides of the	include autoimmune diseases
	invention (including antibodies	(e.g., rheumatoid arthritis,
	and agonists or antagonists of	systemic lupus erythematosis,
	the invention) to regulate	multiple sclerosis and/or as
	NFAT transcription factors and	described below),
	modulate expression of genes	immunodeficiencies (e.g., as
	involved in	described below), boosting a T
	immunomodulatory functions.	cell-mediated immune
	Exemplary assays for	response, and suppressing a T
	transcription through the	cell-mediated immune
	NFAT response element that	response. Additional highly
,	may be used or routinely	preferred indications include
	modified to test NFAT-	inflammation and
	response element activity of	inflammatory disorders. An
	polypeptides of the invention	additional highly preferred
	(including antibodies and	indication is infection (e.g., an
	agonists or antagonists of the	infectious disease as described
	invention) include assays	below under "Infectious
	disclosed in Berger et al., Gene	Disease"). Preferred
	66:1-10 (1998); Cullen and	indications include neoplastic
	Malm, Methods in Enzymol	diseases (e.g., leukemia,
	216:362-368 (1992); Henthorn	lymphoma, and/or as described
	et al., Proc Natl Acad Sci USA	below under
	85:6342-6346 (1988);	"Hyperproliferative
	Aramburu et al., J Exp Med	Disorders"). Preferred
 	182(3):801-810 (1995); De	indications include neoplasms
	Boer et al., Int J Biochem Cell	and cancers, such as, for
	Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,

				Fraser et al., Eur J Immunol	and prostate, breast, lung,
				29(3):838-844 (1999); and	colon, pancreatic, esophageal,
			-	Yeseen et al., J Biol Chem	stomach, brain, liver and
				268(19):14285-14293 (1993),	urinary cancer. Other preferred
				the contents of each of which	indications include benign
				are herein incorporated by	dysproliferative disorders and
				reference in its entirety. NK	pre-neoplastic conditions, such
				cells that may be used	as, for example, hyperplasia,
				according to these assays are	metaplasia, and/or dysplasia.
_				publicly available (e.g.,	Preferred indications also
				through the ATCC).	include anemia, pancytopenia,
				Exemplary human NK cells	leukopenia, thrombocytopenia,
				that may be used according to	Hodgkin's disease, acute
				these assays include the NK-	lymphocytic anemia (ALL),
				YT cell line, which is a human	plasmacytomas, multiple
				natural killer cell line with	myeloma, Burkitt's lymphoma,
				cytolytic and cytotoxic	arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel
					disease, sepsis, neutropenia,
			**		neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
	-				diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HCUIM65	573	Activation of	Assays for the activation of	Highly preferred indications
			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications

include blood disorders (e.g.,	"" "" "" "" "" "" "" "" "" "" "" "" ""	Related Disorders" and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below), and	immunodeficiencies (e.g., as	described below). An	additional highly preferred	indication is infection (e.g.,	AIDS, and/or an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	Lancock lives and a
be used or routinely modified	to assess the ability of	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1000) the contents of each of
immune cells (such	cells)	./																											
					-																								
										_				_													_		

			which are herein incorporated	esophageal, stomach, brain,
			by reference in its entirety.	liver and urinary cancer. Other
			NK cells that may be used	preferred indications include
			according to these assays are	benign dysproliferative
			publicly available (e.g.,	disorders and pre-neoplastic
_			through the ATCC).	conditions, such as, for
			Exemplary NK cells that may	example, hyperplasia,
			be used according to these	metaplasia, and/or dysplasia.
	_		assays include the NK-YT cell	Preferred indications also
			line, which is a human natural	include anemia, pancytopenia,
_			killer cell line with cytolytic	leukopenia, thrombocytopenia,
			and cytotoxic activity.	Hodgkin's disease, acute
	_			lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS, granulomatous
				disease, inflammatory bowel
				disease, sepsis, neutropenia,
				neutrophilia, psoriasis,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
				suppression of immune
				reactions to transplanted
				organs, asthma and allergy.
HCUIM65	573	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
-		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
	•	immune cells (such	art and may be used or	production. An alternative
		as natural killer	routinely modified to assess	highly preferred embodiment

the ability of polypeptides of the invention includes a antibodies and agonists or antigonisis of the invention) to receasing) TNF alpha antigonisis of the invention of genes involved cregulate serum response factors and modulate the disorders (e.g., as described expression of genes involved in growth and upregulate the function of growth-related function of growth-related function of growth-related plsorders, and/or genes in many cell types. Exemplay assays for transcription through the SRE cativity of the polypeptides of the invention) including antibodes sclerosis and/or as described and agonists or antigonists of the polypeptides of the invention) including antibodes sclerosis and/or as described and agonists or antigonists of below), immunodeficiencies the invention) including antibodes sclerosis and/or as described and agonists or antigonists of below), immunodeficiencies that may be not state or too Natl Acad St. USA mighty preferred indications 85:624-564 (1988). Benson cet al., Immunol 153(9):362-117 patients with remanded supply preferred indications in chain or patients with remanded supply preferred indications is elby preferred indications is elby. Indithy preferred indications is elby preferred indications is elby preferred indications is elby preferred indications indications is elby preferred indications is elby and many elby preferred indications is elby and many elby preferred indications is elby and many elby preferred indications is elby preferred indications is elby preferred indications is elby preferred indications is elby preferred indications in the preferred indications is elby preferred indications in the preferred indications in
cells).

			according to these assays are	(e.g., leukemia, lymphoma,
		_	publicly available (e.g.,	and/or as described below
	·		through the ATCC).	under "Hyperproliferative
			Exemplary T cells that may be	Disorders"). Additionally,
			used according to these assays	highly preferred indications
			include the NK-YT cell line,	include neoplasms and
			which is a human natural killer	cancers, such as, for example,
	_	-	cell line with cytolytic and	leukemia, lymphoma,
			cytotoxic activity.	melanoma, glioma (e.g.,
				malignant glioma), solid
	_			tumors, and prostate, breast,
				lung, colon, pancreatic,
	_			esophageal, stomach, brain,
	-			liver and urinary cancer. Other
	_			preferred indications include
				benign dysproliferative
				disorders and pre-neoplastic
_				conditions, such as, for
	-	-		example, hyperplasia,
				metaplasia, and/or dysplasia.
	, , - '			Preferred indications include
				anemia, pancytopenia,
	,—			leukopenia, thrombocytopenia,
		_		Hodgkin's disease, acute
_	-	 -		lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
_	-			arthritis, AIDS, granulomatous
				disease, inflammatory bowel
				disease, neutropenia,
				neutrophilia, psoriasis,

suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkins lymphoma, non-Hodgkins lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include
	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or
	Activation of transcription through GAS response element in immune cells (such as T-cells).
	573
	HCUIM65

		GAS-response element activity	disorders and pre-neoplastic
		of polypeptides of the	conditions, such as, for
		invention (including antibodies	example, hyperplasia,
		and agonists or antagonists of	metaplasia, and/or dysplasia.
		the invention) include assays	Preferred indications include
		disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
-		66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
		Malm, Methods in Enzymol	lupus erythematosis, multiple
		216:362-368 (1992); Henthorn	sclerosis and/or as described
	-	et al., Proc Natl Acad Sci USA	below), immunodeficiencies
		85:6342-6346 (1988);	(e.g., as described below),
		Matikainen et al., Blood	boosting a T cell-mediated
		93(6):1980-1991 (1999); and	immune response, and
	3	Henttinen et al., J Immunol	suppressing a T cell-mediated
		155(10):4582-4587 (1995), the	immune response. Additional
		contents of each of which are	preferred indications include
		herein incorporated by	inflammation and
-		reference in its entirety.	inflammatory disorders.
		Exemplary human T cells,	Highly preferred indications
		such as the SUPT cell line, that	include blood disorders (e.g.,
	-	may be used according to these	as described below under
		assays are publicly available	"Immune Activity", "Blood-
		(e.g., through the ATCC).	Related Disorders", and/or
			"Cardiovascular Disorders"),
	-		and infection (e.g., viral
			infections, tuberculosis,
			infections associated with
			chronic granulomatosus
			disease and malignant
			osteoporosis, and/or an
			infectious disease as described

				below under "Infectious
				Disease"). An additional
				preferred indication is
				idiopathic pulmonary fibrosis.
_				Preferred indications include
				anemia, pancytopenia,
				leukopenia, thrombocytopenia,
				acute lymphocytic anemia
				(ALL), plasmacytomas,
				multiple myeloma, arthritis,
				AIDS, granulomatous disease,
				inflammatory bowel disease,
				sepsis, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease, and
STOCKING!				asthma and allergy.
HCWDS/2	574	Regulation of	Assays for the regulation of	A highly preferred
		transcription of	transcription of Malic Enzyme	indication is diabetes mellitus.
		Malic Enzyme in	are well-known in the art and	An additional highly preferred
		adipocytes	may be used or routinely	indication is a complication
			modified to assess the ability	associated with diabetes (e.g.,
			of polypeptides of the	diabetic retinopathy, diabetic
_			invention (including antibodies	nephropathy, kidney disease
	_		and agonists or antagonists of	(e.g., renal failure,
			the invention) to regulate	nephropathy and/or other
			transcription of Malic Enzyme,	diseases and disorders as

a key enzyme in lipogenesis.	described in the "Renal
Malic enzyme is involved in	Disorders" section below),
lipogenesisand its expression is	diabetic neuropathy, nerve
stimulted by insulin. ME	disease and nerve damage
promoter contains two direct	(e.g., due to diabetic
 repeat (DR1)- like elements	neuropathy), blood vessel
MEp and MEd identified as	blockage, heart disease, stroke,
putative PPAR response	impotence (e.g., due to diabetic
elements. ME promoter may	neuropathy or blood vessel
also responds to AP1 and other	blockage), seizures, mental
transcription factors.	confusion, drowsiness,
Exemplary assays that may be	nonketotic hyperglycemic-
 used or routinely modified to	hyperosmolar coma,
 test for regulation of	cardiovascular disease (e.g.,
transcription of Malic Enzyme	heart disease, atherosclerosis,
(in adipoocytes) by	microvascular disease,
polypeptides of the invention	hypertension, stroke, and other
 (including antibodies and	diseases and disorders as
 agonists or antagonists of the	described in the
invention) include assays	"Cardiovascular Disorders"
 disclosed in: Streeper, R.S., et	section below), dyslipidemia,
al., Mol Endocrinol,	endocrine disorders (as
 12(11):1778-91 (1998);	described in the "Endocrine
Garcia-Jimenez, C., et al., Mol	Disorders" section below),
Endocrinol, 8(10):1361-9	neuropathy, vision impairment
(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
Biol Chem, 274(25):17997-	blindness), ulcers and impaired
8004 (1999); Ijpenberg, A., et	wound healing, and infection
al., J Biol Chem,	(e.g., infectious diseases and
272(32):20108-20117 (1997);	disorders as described in the
Berger, et al., Gene 66:1-10	"Infectious Diseases" section

				(1988): and. Cullen. B., et al.,	below, especially of the
				Methods in Enzymol.	urinary tract and skin), carpal
				216:362–368 (1992), the	tunnel syndrome and
				contents of each of which is	Dupuytren's contracture).
				herein incorporated by	An additional highly preferred
				reference in its entirety.	indication is obesity and/or
				Hepatocytes that may be used	complications associated with
				according to these assays are	obesity. Additional highly
				publicly available (e.g.,	preferred indications include
				through the ATCC) and/or	weight loss or alternatively,
				may be routinely generated.	weight gain. Aditional
				Exemplary hepatocytes that	highly preferred indications are
				may be used according to these	complications associated with
				assays includes the H4IIE rat	insulin resistance.
				liver hepatoma cell line.	
	HCWGU37	575	Calcium flux in	Assays for measuring calcium	Preferred embodiments of the
_			chondrocytes	flux are well-known in the art	invention include using
				and may be used or routinely	polypeptides of the invention
				modified to assess the ability	(or antibodies, agonists, or
				of polypeptides of the	antagonists thereof) in
				invention (including antibodies	detection, diagnosis,
				and agonists or antagonists of	prevention, and/or treatment of
				the invention) to mobilize	Bone and Cartilage Diseases,
				calcium. Cells normally have	including but not limited to
				very low concentrations of	Arthritis, Cartilige repair, Bone
				cytosolic calcium compared to	Repair, Osteoporosis, and
				much higher extracellular	related tumors including
				calcium. Extracellular factors	chondrosarcomas,
				can cause an influx of calcium,	chondroblastomas, and
•				leading to activation of	chondromas.
				calcium responsive signaling	

	A highly preferred indication is diabetes mellitus.	Additional highly preferred indications include	complications associated with diabetes (e.g., diabetic
pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux in chondrocytes include assays disclosed in: Asada S, et al., Inflamm Res, 50(1):19-23 (2001); Schwartz Z, et al., J Bone Miner Res, 6(7):709-718 (1991); Iannotti JP, et al., J Bone Joint Surg Am, 67(1): 113-120 (1985); Sullivan E., et al., Methods Mol Biol 1999; 114:125-133 (1999), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include bovine chondrocytes.	Assays for the regulation of transcription through the	DMEF1 response element are	be used or routinely modified to assess the ability of
	Regulation of transcription via	DMEF1 response	adipocytes and pre-
	576		
	HCWKC15		
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including antibodies and agonists of the invention of including antibodies and agonists of the e.g., renal failure, invention) to activate the phytopathy, kidney disease agonists of the invention) to activate the described in the "Renal containing the CLUT4 promoter) and to regulate insulin production. The DMEF1 response element is present in the GLUT4 promoter and binds to MEF2 promoter and promoter and another response element activity (in dispersion) and adposites of the invention) include assays that microvascular Disorders and agonists or anagonists or	Γ							-																							
polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the DMEF I response element in a reporter construct (such as that containing the GLUT4 promoter) and to regulate insulin production. The DMEF I response element is present in the GLUT4 promoter and binds to MEF2 transcription factor and another transcription factor that is required for insulin regulation of Glut4 expression in skeletal muscle. GLUT4 is the primary insulin-responsive glucose transporter in fat and muscle tissue. Exemplary assays that may be used or routinely modified to test for DMEF1 response element activity (in adipocytes and pre-adipocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed inflation S. et al., J Biol Chem, 273(23):1488-92 (1998): Mons. S. et al., J Biol Chem, S. et al., J Biol Chem, S. et al., Biol	retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel			neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and
	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to activate the	DMEF1 response element in a	reporter construct (such as that	containing the GLUT4	promoter) and to regulate	insulin production. The	DMEF1 response element is	present in the GLUT4	promoter and binds to MEF2	transcription factor and another	transcription factor that is	required for insulin regulation	of Glut4 expression in skeletal	muscle. GLUT4 is the primary	insulin-responsive glucose	transporter in fat and muscle	tissue. Exemplary assays that	may be used or routinely	modified to test for DMEF1	response element activity (in	adipocytes and pre-adipocytes)	by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed inThai, M.V., et al., J	Biol Chem, 273(23):14285-92	(1998); Mora, S., et al., J Biol
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Chem, 275(21):16323-8 blindness), ulcers and impaired	(2000); Liu, M.L., et al., J Biol wound healing, and infection	Chem, 269(45):28514-21 (e.g., infectious diseases and	a 30-	base pair regulatory element "Infectious Diseases" section	and novel DNA binding below, especially of the	protein that regulates the urinary tract and skin). An	in	m.	2000 Aug 4;275(31):23666-73; complications associated with	 •	Methods in Enzymol. weight loss or alternatively,	216:362–368 (1992), the weight gain. Additional highly	contents of each of which is preferred indications are	herein incorporated by complications associated with	reference in its entirety. insulin resistance.	Adipocytes and pre-adipocytes	that may be used according to	these assays are publicly	available (e.g., through the	ATCC) and/or may be	routinely generated.	Exemplary cells that may be	used according to these assays	include the mouse 3T3-L1 cell	line which is an adherent	mouse preadipocyte cell line.	Mouse 3T3-L1 cells are a	continuous substrain of 3T3	
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				clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.	
HCWKC15	315	576	Activation of transcription	Assays for the activation of transcription through the	A highly preferred indication is obesity and/or complications
	_		through cAMP	cAMP response element are	associated with obesity.
	-		response element	well-known in the art and may	Additional highly preferred
			(CKE) in pre-	be used or routinely modified	indications include weight loss
			aupocytes.	polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
				invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
_			_	in a wide variety of cell	(e.g., renal failure,
	,			functions. For example, a	nephropathy and/or other
				3T3-L1/CRE reporter assay	diseases and disorders as
_			-	may be used to identify factors	described in the "Renal
				that activate the cAMP	Disorders" section below),
				signaling pathway. CREB	diabetic neuropathy, nerve
				plays a major role in	disease and nerve damage
				adipogenesis, and is involved	(e.g., due to diabetic
				in differentiation into	neuropathy), blood vessel
				adipocytes. CRE contains the	blockage, heart disease, stroke,
				binding sequence for the	impotence (e.g., due to diabetic
				transcription factor CREB	neuropathy or blood vessel
				(CRE binding protein).	blockage), seizures, mental

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confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	Additional highly preferred	indications are complications	associated with insulin	resistance.		
Exemplary assays for	transcription through the	cAMP response element that	may be used or routinely	modified to test cAMP-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch	et al., Mol Cell Biol	20(3):1008-1020 (2000); and	Klemm et al., J Biol Chem	273:917-923 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. Pre-	adipocytes that may be used	according to these assays are	publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary mouse adipocyte	cells that may be used	according to these assays
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				include 3T3-L1 cells. 3T3-L1	
				is an adherent mouse	
				preadipocyte cell line that is a	
				continuous substrain of 3T3	
				fibroblast cells developed	
				through clonal isolation and	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
				conditions known in the art.	
	HCWKC15	925	Activation of	Assays for the activation of	A highly preferred indication
			transcription	transcription through the	is obesity and/or complications
			through serum	Serum Response Element	associated with obesity.
			response element in	(SRE) are well-known in the	Additional highly preferred
			pre-adipocytes.	art and may be used or	indications include weight loss
				routinely modified to assess	or alternatively, weight gain.
				the ability of polypeptides of	An additional highly preferred
				the invention (including	indication is diabetes mellitus.
				antibodies and agonists or	An additional highly preferred
				antagonists of the invention) to	indication is a complication
				regulate the serum response	associated with diabetes (e.g.,
				factors and modulate the	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in growth. Exemplary assays	(e.g., renal failure,
				for transcription through the	nephropathy and/or other
				SRE that may be used or	diseases and disorders as
				routinely modified to test SRE	described in the "Renal
7				activity of the polypeptides of	Disorders" section below),
				the invention (including	diabetic neuropathy, nerve
				antibodies and agonists or	disease and nerve damage
				antagonists of the invention)	(e.g., due to diabetic

				include assays disclosed in	neuropathy), blood vessel
				Berger et al., Gene 66:1-10	blockage, heart disease, stroke,
				(1998); Cullen and Malm,	impotence (e.g., due to diabetic
				Methods in Enzymol 216:362-	neuropathy or blood vessel
				368 (1992); Henthorn et al.,	blockage), seizures, mental
				Proc Natl Acad Sci USA	confusion, drowsiness,
		1		85:6342-6346 (1988); and	nonketotic hyperglycemic-
				Black et al., Virus Genes	hyperosmolar coma,
				12(2):105-117 (1997), the	cardiovascular disease (e.g.,
				content of each of which are	heart disease, atherosclerosis,
				herein incorporated by	microvascular disease,
			_	reference in its entirety. Pre-	hypertension, stroke, and other
				adipocytes that may be used	diseases and disorders as
				according to these assays are	described in the
				publicly available (e.g.,	"Cardiovascular Disorders"
				through the ATCC) and/or	section below), dyslipidemia,
				may be routinely generated.	endocrine disorders (as
				Exemplary mouse adipocyte	described in the "Endocrine
				cells that may be used	Disorders" section below),
				according to these assays	neuropathy, vision impairment
				include 3T3-L1 cells. 3T3-L1	(e.g., diabetic retinopathy and
				is an adherent mouse	blindness), ulcers and impaired
				preadipocyte cell line that is a	wound healing, and infection
				continuous substrain of 3T3	(e.g., infectious diseases and
				fibroblast cells developed	disorders as described in the
				through clonal isolation and	"Infectious Diseases" section
				undergo a pre-adipocyte to	below). Additional highly
				adipose-like conversion under	preferred indications are
				appropriate differentiation	complications associated with
•				conditions known in the art.	insulin resistance.
I	HCWKC15	576	Activation of	Assays for the activation of	Highly preferred indications

transcription	transcription through the	include asthma, allergy,	
through GAS	Gamma Interferon Activation	hypersensitivity reactions,	
response element in	Site (GAS) response element	inflammation, and	
immune cells (such	are well-known in the art and	inflammatory disorders.	
 as eosinophils).	may be used or routinely	Additional highly preferred	
	modified to assess the ability	indications include immune	
	of polypeptides of the	and hematopoietic disorders	
	invention (including antibodies	(e.g., as described below under	
	and agonists or antagonists of	"Immune Activity", and	
-	the invention) to modulate	"Blood-Related Disorders"),	
	gene expression (commonly	autoimmune diseases (e.g.,	
	via STAT transcription factors)	rheumatoid arthritis, systemic	
	involved in a wide variety of	lupus erythematosis, Crohn"s	
	cell functions. Exemplary	disease, multiple sclerosis	
	assays for transcription	and/or as described below),	
-	through the GAS response	immunodeficiencies (e.g., as	
	element that may be used or	described below), boosting an	
	routinely modified to test	eosinophil-mediated immune	
	GAS-response element activity	response and, alternatively,	
	of polypeptides of the	suppressing an eosinophil-	
	invention (including antibodies	mediated immune response.	
	and agonists or antagonists of		
	the invention) include assays		
	disclosed in Berger et al., Gene		
	66:1-10 (1998); Cullen and		
	Malm, Methods in Enzymol		
	216:362-368 (1992); Henthorn		
	et al., Proc Natl Acad Sci USA		
	85:6342-6346 (1988);		
	Matikainen et al., Blood		
	93(6):1980-1991 (1999); and		

Henttinen et al., J Immunol	155(10):4582-4587 (1995); the	contents of each of which are	herein incorporated by	reference in its entirety.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to activate or	inhibit activation of immune	cells include assays disclosed	and/or cited in: Mayumi M.,	"EoL-1, a human eosinophilic	cell line" Leuk Lymphoma;	Jun;7(3):243-50 (1992);	Bhattacharya S, "Granulocyte	macrophage colony-	stimulating factor and	interleukin-5 activate STAT5	and induce CIS1 mRNA in	human peripheral blood	eosinophils" Am J Respir Cell	Mol Biol; Mar;24(3):312-6	(2001); and, Du J, et al.,	"Engagement of the CrkL	adapter in interleukin-5	signaling in eosinophils" J Biol	Chem; Oct 20;275(42):33167-
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			75 (2000); the contents of each of which are herein	
			incorporated by reference in its	
			entirety. Exemplary cells that	
			may be used according to these	
			assays include eosinophils.	
			Eosinophils are a type of	
			immune cell important in the	
			late stage of allergic reactions;	
			they are recruited to tissues	
			and mediate the inflammtory	
			response of late stage allergic	
			reaction. Increases in GAS	
			mediated transcription in	
			eosinophils is typically a result	
 			of STAT activation, normally a	
			direct consequence of	
			interleukin or other cytokine	
			receptor stimulation (e.g. IL3,	
			IL5 or GMCSF).	
HCWKC15	576	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include asthma, allergy,
		through NFKB	NFKB response element are	hypersensitivity reactions, and
		response element in	well-known in the art and may	inflammation. Preferred
		immune cells (such	be used or routinely modified	indications include infection
		as EOL1 cells).	to assess the ability of	(e.g., an infectious disease as
	2008		polypeptides of the invention	described below under
	-		(including antibodies and	"Infectious Disease"),
			agonists or antagonists of the	immunological disorders,
			invention) to regulate NFKB	inflammation and
			transcription factors and	inflammatory disorders (e.g.,

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as described below under	"Immune Activity", and	"Blood-Related Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below).																				
modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	For example, a reporter assay	(which measures increases in	transcription inducible from a	NFkB responsive element in	EOL-1 cells) may link the
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																_														

				NFKB element to a repeorter	
				gene and binds to the NFKB	
				transcription factor, which is	
				upregulated by cytokines and	
				other factors. Exemplary	
		-		immune cells that may be used	
				according to these assays	
				include eosinophils such as the	
				human EOL-1 cell line of	
				eosinophils. Eosinophils are a	
				type of immune cell important	
				in the allergic responses; they	
				are recruited to tissues and	
				mediate the inflammtory	
				response of late stage allergic	
				reaction. Eol-1 is a human	
				eosinophil cell line.	
	HCWKC15	276	Activation of	This reporter assay measures	Highly preferred indications
			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
-				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or

	the invention (including	"Cardiovascular Disorders").	_
	antibodies and agonists or	Preferred indications include	
	antagonists of the invention) to	autoimmune diseases (e.g.,	
	regulate GATA3 transcription	rheumatoid arthritis, systemic	
	factors and modulate	lupus erythematosis, multiple	
	expression of mast cell genes	sclerosis and/or as described	
	important for immune response	below) and	
	development. Exemplary	immunodeficiencies (e.g., as	
	assays for transcription	described below). Preferred	
	through the GATA3 response	indications include neoplastic	
	element that may be used or	diseases (e.g., leukemia,	_
	routinely modified to test	lymphoma, melanoma,	
	GATA3-response element	prostate, breast, lung, colon,	
	activity of polypeptides of the	pancreatic, esophageal,	
	invention (including antibodies	stomach, brain, liver, and	
	and agonists or antagonists of	urinary tract cancers and/or as	
	the invention) include assays	described below under	
	disclosed in Berger et al., Gene	"Hyperproliferative	
	66:1-10 (1998); Cullen and	Disorders"). Other preferred	
	Malm, Methods in Enzymol	indications include benign	
-	216:362-368 (1992); Henthorn	dysproliferative disorders and	
	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such	
	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,	
	et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.	
	Quant Biol 64:563-571 (1999);	Preferred indications include	
	Rodriguez-Palmero et al., Eur	anemia, pancytopenia,	
	J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,	
	(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,	
	Cell 89(4):587-596 (1997); and	acute lymphocytic anemia	
	<u>l</u> o	(ALL), plasmacytomas,	
	14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's	_

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			Louis in the market of all all	iymphoma, arumus, AiDS,
			nerein incorporated by	granulomatous disease,
			reference in its entirety. Mast	inflammatory bowel disease,
			cells that may be used	sepsis, neutropenia,
			according to these assays are	neutrophilia, psoriasis,
			publicly available (e.g.,	suppression of immune
			through the ATCC).	reactions to transplanted
			Exemplary human mast cells	organs and tissues, hemophilia,
			that may be used according to	hypercoagulation, diabetes
			these assays include the HMC-	mellitus, endocarditis,
			1 cell line, which is an	meningitis, and Lyme Disease.
			immature human mast cell line	
			established from the peripheral	
			blood of a patient with mast	
			cell leukemia, and exhibits	
			many characteristics of	
			immature mast cells.	
HCWKC15	276	Activation of	This reporter assay measures	Highly preferred indications
		transcription	activation of the NFAT	include allergy, asthma, and
		through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
		response element in	human mast cell line.	indications include infection
		immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
		as mast cells).	cells has been linked to	described below under
			cytokine and chemokine	"Infectious Disease"), and
			production. Assays for the	inflammation and
			activation of transcription	inflammatory disorders.
			through the Nuclear Factor of	Preferred indications also
			Activated T cells (NFAT)	include blood disorders (e.g.,
			response element are well-	as described below under
			known in the art and may be	"Immune Activity", "Blood-
			used or routinely modified to	Related Disorders", and/or

assess the ability of	"Cardiovascular Disorders")
polypeptides of the invention	Preferred indications include
(including antibodies and	autoimmune diseases (e.g.,
agonists or antagonists of the	rheumatoid arthritis, systemic
invention) to regulate NFAT	lupus erythematosis, multiple
transcription factors and	sclerosis and/or as described
modulate expression of genes	below) and
involved in	immunodeficiencies (e.g., as
immunomodulatory functions.	described below). Preferred
Exemplary assays for	indications include neoplastic
transcription through the	diseases (e.g., leukemia,
NFAT response element that	lymphoma, melanoma,
may be used or routinely	prostate, breast, lung, colon,
modified to test NFAT-	pancreatic, esophageal,
response element activity of	stomach, brain, liver, and
polypeptides of the invention	urinary tract cancers and/or as
(including antibodies and	described below under
agonists or antagonists of the	"Hyperproliferative
invention) include assays	Disorders"). Other preferred
disclosed in Berger et al., Gene	indications include benign
66:1-10 (1998); Cullen and	dysproliferative disorders and
Malm, Methods in Enzymol	pre-neoplastic conditions, such
216:362-368 (1992); Henthorn	as, for example, hyperplasia,
et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
85:6342-6346 (1988); De Boer	Preferred indications include
et al., Int J Biochem Cell Biol	anemia, pancytopenia,
31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
et al., J Immunol	leukemias, Hodgkin's disease,
 165(12):7215-7223 (2000);	acute lymphocytic anemia
Hutchinson and McCloskey, J	(ALL), plasmacytomas,
Biol Chem 270(27):16333-	multiple myeloma, Burkitt's

			16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
			al., J Exp Med 188:527-537	granulomatous disease,
			(1998), the contents of each of	inflammatory bowel disease,
			which are herein incorporated	sepsis, neutropenia,
			by reference in its entirety.	neutrophilia, psoriasis,
			Mast cells that may be used	suppression of immune
			according to these assays are	reactions to transplanted
			publicly available (e.g.,	organs and tissues, hemophilia,
			through the ATCC).	hypercoagulation, diabetes
			Exemplary human mast cells	mellitus, endocarditis,
			that may be used according to	meningitis, and Lyme Disease.
			these assays include the HMC-	
			1 cell line, which is an	
			immature human mast cell line	
			established from the peripheral	
			blood of a patient with mast	
			cell leukemia, and exhibits	
			many characteristics of	
			immature mast cells.	
HCWKC15	576	Activation of	This reporter assay measures	Highly preferred indication
		transcription	activation of the NFkB	includes allergy, asthma, and
		through NFKB	signaling pathway in HMC-1	rhinitis. Additional highly
		response element in	human mast cell line.	preferred indications include
		immune cells (such	Activation of NFkB in mast	infection (e.g., an infectious
		as mast cells).	cells has been linked to	disease as described below
			production of certain	under "Infectious Disease"),
			cytokines, such as IL-6 and IL-	and inflammation and
			9. Assays for the activation of	inflammatory disorders.
			transcription through the	Preferred indications include
			NFKB response element are	immunological and
			well-known in the art and may	hempatopoietic disorders (e.g.,

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	as described below under	"Immune Activity", and	"Blood-Related Disorders").	Preferred indications also	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications also include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancer, such as, for	example, leukemia, lymphoma,	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary tract cancers and	as described below under	"Hyperproliferative	Disorders".		
1 2 2 1	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Stassen	et al, J Immunol 166(7):4391-8	(2001); and Marquardt and	Walker, J Allergy Clin	Immunol 105(3):500-5 (2000),	the contents of each of which
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				reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast	
				cell leukemia, and exhibits many characteristics of immature mast cells.	
	HCWKC15	576	Activation of	Assays for the activation of	Highly preferred indications
			transcription	transcription through the	include allergy, asthma, and
			through STAT6	Signal Transducers and	rhinitis. Additional highly
			response element in	Activators of Transcription	preferred indications include
			immune cells (such	(STAT6) response element in	infection (e.g., an infectious
			as mast cells).	immune cells (such as in the	disease as described below
				human HMC-1 mast cell line)	under "Infectious Disease"),
				are well-known in the art and	and inflammation and
				may be used or routinely	inflammatory disorders.
				modified to assess the ability	Preferred indications also
				of polypeptides of the	include hematopoietic and
				invention (including antibodies	immunological disorders (e.g.,
				and agonists or antagonists of	as described below under
				the invention) to regulate	"Immune Activity", "Blood-
_				STAT6 transcription factors	Related Disorders", and/or
				and modulate the expression of	"Cardiovascular Disorders"),

	multiple genes. Exemplary	autoimmune diseases (e.g.,
	assays for transcription	rheumatoid arthritis, systemic
	through the STAT6 response	lupus erythematosis, multiple
	element that may be used or	sclerosis and/or as described
	routinely modified to test	below), and
	STAT6 response element	immunodeficiencies (e.g., as
	activity of the polypeptides of	described below). Preferred
-	the invention (including	indications include neoplastic
	antibodies and agonists or	diseases (e.g., leukemia,
-	antagonists of the invention)	lymphoma, melanoma, and/or
	include assays disclosed in	as described below under
	Berger et al., Gene 66:1-10	"Hyperproliferative
	(1998); Cullen and Malm,	Disorders"). Preferred
	Methods in Enzymol 216:362-	indications include neoplasms
	368 (1992); Henthorn et al.,	and cancer, such as, for
	Proc Natl Acad Sci USA	example, leukemia, lymphoma,
	85:6342-6346 (1988);	melanoma, and prostate,
	Sherman, Immunol Rev	breast, lung, colon, pancreatic,
	179:48-56 (2001); Malaviya	esophageal, stomach, brain,
	and Uckun, J Immunol	liver and urinary cancer. Other
	168:421-426 (2002); Masuda	preferred indications include
	et al., J Biol Chem	benign dysproliferative
	275(38):29331-29337 (2000);	disorders and pre-neoplastic
	and Masuda et al., J Biol Chem	
	276:26107-26113 (2001), the	example, hyperplasia,
	contents of each of which are	metaplasia, and/or dysplasia.
	herein incorporated by	Preferred indications include
	reference in its entirety. Mast	hematopoietic and
	cells that may be used	immunological disorders such
	according to these assays are	as arthritis, AIDS,
	publicly available (e.g.,	granulomatous disease,

			Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells	sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
HCWKC15	576	Activation of transcription through NFKB response element in immune cells (such as basophils).	This reporter assay measures activation of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the	Highly preferred indication includes allergy, asthma, and rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammatory disorders. Preferred indications include immunological and hempatopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"). Preferred indications also include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,
			immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that	include autoimmune diseas (e.g., rheumatoid arthritis, systemic lupus erythematos multiple sclerosis and/or as

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described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications also include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancer, such as, for	example, leukemia, lymphoma,	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary tract cancers and	as described below under	"Hyperproliferative	Disorders".											
may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone	et al, Int Arch Allergy	Immunol 114(3):207-17	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Basophils that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human basophil	cell lines that may be used	according to these assays	include Ku812, originally	established from a patient with	chronic myelogenous	leukemia. It is an immature	prebasophilic cell line that can	be induced to differentiate into
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				mature basophils.	
	HCWKC15	576	Activation of	Assays for the activation of	Highly preferred indications
			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response element in	cells (NFAT) response element	"Immune Activity", "Blood-
			immune cells (such	are well-known in the art and	Related Disorders", and/or
			as natural killer	may be used or routinely	"Cardiovascular Disorders").
			cells).	modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				immunomodulatory functions.	cell-mediated immune
_				Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
				NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
				response element activity of	inflammatory disorders. An
				polypeptides of the invention	additional highly preferred
				(including antibodies and	indication is infection (e.g., an
				agonists or antagonists of the	infectious disease as described
				invention) include assays	below under "Infectious
				disclosed in Berger et al., Gene	Disease"). Preferred
				66:1-10 (1998); Cullen and	indications include neoplastic
				Malm, Methods in Enzymol	diseases (e.g., leukemia,
			-	216:362-368 (1992); Henthorn	lymphoma, and/or as described
				et al., Proc Natl Acad Sci USA	below under

"Hyperproliferative Disorders") Preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	and prostate, breast, lung,	colon, pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,
85:6342-6346 (1988); Aramburu et al. I Exp. Med	182(3):801-810 (1995); De	Boer et al., Int J Biochem Cell	Biol 31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by	reference in its entirety. NK	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human NK cells	that may be used according to	these assays include the NK-	YT cell line, which is a human	natural killer cell line with	cytolytic and cytotoxic	activity.								
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					asthma and allergy.
	HCWKC15	576	Activation of	Assays for the activation of	Highly preferred indications
			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
		_	immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as natural killer	to assess the ability of	as described below under
		_	cells).	polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
-				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
_				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
				NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
				invention) include assays	Highly preferred indications
				disclosed in Berger et al., Gene	include neoplastic diseases
				66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
				Malm, Methods in Enzymol	lymphoma, and/or as described
				216:362-368 (1992); Henthorn	below under
			-	et al., Proc Natl Acad Sci USA	"Hyperproliferative
				85:6342-6346 (1988); Valle	Disorders"). Highly preferred
				Blazquez et al, Immunology	indications include neoplasms

			90(3):455-460 (1997):	and cancers such as for
			Aramburan et al. I Exn Med	example melanoma renal cell
			82(3):801-810 (1995); and	carcinoma, leukemia.
	- 45		Fraser et al., 29(3):838-844	lymphoma, and prostate,
			(1999), the contents of each of	breast, lung, colon, pancreatic,
			which are herein incorporated	esophageal, stomach, brain,
			by reference in its entirety.	liver and urinary cancer. Other
			NK cells that may be used	preferred indications include
			according to these assays are	benign dysproliferative
			publicly available (e.g.,	disorders and pre-neoplastic
			through the ATCC).	conditions, such as, for
	_		Exemplary NK cells that may	example, hyperplasia,
			be used according to these	metaplasia, and/or dysplasia.
			assays include the NK-YT cell	Preferred indications also
			line, which is a human natural	include anemia, pancytopenia,
			killer cell line with cytolytic	leukopenia, thrombocytopenia,
			and cytotoxic activity.	Hodgkin's disease, acute
				lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
-	-			arthritis, AIDS, granulomatous
				disease, inflammatory bowel
				disease, sepsis, neutropenia,
				neutrophilia, psoriasis,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
			-	suppression of immune
				reactions to transplanted
				organs, asthma and allergy.
HCWKC15	576	Activation of	Assays for the activation of	A preferred embodiment of

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the invention includes a	method for inhibiting (e.g.,	reducing) TNF alpha	production. An alternative	highly preferred embodiment	of the invention includes a	method for stimulating (e.g.,	increasing) TNF alpha	production. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn's disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in
transcription through the	Serum Response Element	(SRE) are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate serum response	factors and modulate the	expression of genes involved	in growth and upregulate the	function of growth-related	genes in many cell types.	Exemplary assays for	transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,
transcription	through serum	response element in	immune cells (such	as natural killer	cells).																									
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patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple
Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.																	
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_					myeloma Burkitt's lymphoma
					arthritis, AIDS, granulomatous
		-			disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
		-			reactions to transplanted
					organs and tissues, hemophilia,
	-				hypercoagulation, diabetes
					mellitus, endocarditis,
			-		meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
			,		is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
<u></u>	HCWKC15	276	Activation of	Assays for the activation of	Highly preferred indications
			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as natural killer	to assess the ability of	as described below under
			cells).	polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
-				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as

Transcription through the may be used or rountinely modified to test NFKB- response element activity of modified to test NFKB- response element activity of modified to test NFKB- additional highly preferred response element activity of modified to test NFKB- additional highly preferred response element activity of modified to test NFKB- additional highly preferred indications disclosed in Berger et al., Gene agonists or antagonists of the invention include assays are disclosed in Berger et al., Gene et al., Proc Natl Acad Sci USA (1988); Valle Blazquez et al., Exp Med stamburau et al., 1 Exp Med stamburau et al., 1 Exp Med stamburau et al., 29(3):838-844 [1999), the contents of each of which are herein incorporated according to these assays are according to these assays are thrush the Aramplay human NK cells that may be used according to these assays include the NKL Processing a described below, and or an infectious Diseases (e.g., melanoma, leukemia, phyperplaisia, through the ATCC). Exemplay human NK cells armay be used according to these assays include the NKL Preferred indications also	e										_				_												-		
transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NKL	transcription through the NFKB response element that may be used or rountinely modified to test NFKB- response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1982); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al., Immunology 90(3):455-460 (1997); Aramburan et al., 1 Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NKL	described below), and immunodeficiencies (e.g., as	described below). An	additional highly preferred	Indication is infection (e.g., AIDS and/or an infections	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,	lymphoma, and/or as described	below under	W. Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also
		transcription through the NFKB response element that	may be used or rountinely	modified to test NFKB-	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	NK cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human NK cells	that may be used according to	these assays include the NKL
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of S	L L
leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allerey.	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic
natural killer cell line established from the peripheral blood of a patient with large granular lymphocytic leukemia. This IL-2 dependent suspension culture cell line has a morphology resembling that of activated NK cells.	Assays for the activation of transcription through the AP1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element
·	Activation of transcription through AP1 response element in immune cells (such as T-cells).
·	576
	HCWKC15

	activity of polypeptides of the	lupus erythematosis, multiple
	and agonists or antagonists of	scierosis and/or as described
	the invention) include assays	immunodeficiencies (e.g., as
	disclosed in Berger et al., Gene	described below). Additional
	66:1-10 (1988); Cullen and	highly preferred indications
	Malm, Methods in Enzymol	include inflammation and
	216:362-368 (1992); Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
_	272(49):30806-30811 (1997);	lymphoma, and/or as described
	Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
 	29(3):838-844 (1999), the	indications include neoplasms
	contents of each of which are	and cancers, such as, leukemia,
	herein incorporated by	lymphoma, prostate, breast,
	reference in its entirety.	lung, colon, pancreatic,
	Human T cells that may be	esophageal, stomach, brain,
	used according to these assays	liver, and urinary cancer. Other
	are publicly available (e.g.,	preferred indications include
	through the ATCC).	benign dysproliferative
	Exemplary human T cells that	disorders and pre-neoplastic
	may be used according to these	conditions, such as, for
	assays include the SUPT cell	example, hyperplasia,
	line, which is an IL-2 and IL-4	metaplasia, and/or dysplasia.
	responsive suspension-culture	Preferred indications include
	cell line.	arthritis, asthma, AIDS,
 		allergy, anemia, pancytopenia,
		leukopenia, thrombocytopenia,

lg)	ative	ent				7		-		SI	es	_	sis,			as	аТ		T T		pa	tic	enal		ibed		•	- eq	ms	
increasi	An altern	mbodim	ncludes a	ting (e.g.	oduction.	preferre	· •		orders.	ndication	ne disea	arthritis,	rthemato	and/or as		es (e.g.,	boosting	nne	oressing	nne	y preferr	e neoplas	anoma, r	ıkemia,	as descr		e	y prefer	e neoplas	as, for
stimulating (e.g., increasing)	IL-2 production. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting (e.g.,	reducing) IL-2 production.	Additional highly preferred	indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response. Highly preferred	indications include neoplastic	diseases (e.g., melanoma, renal	cell carcinoma, leukemia,	lymphoma, and/or as described	ıder	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for
stimulat	IL-2 pro	highly p	of the in	method	reducing	Addition	indicatic	inflamm	inflamm	Highly p	include	(e.g., rhe	systemic	multiple	describe	immuno	describe	cell-med	response	cell-med	response	indicatio	diseases	cell carci	lymphon	below under	"Hyperp	Disorder	indicatio	and canc
., Gene	and	lou	nthorn	i USA			327	munol); and	hem	•	h are		П		s are			ls that	o these	cell	uo								
rger et a	; Cullen	s in Enzy	992); He	l Acad So	(1988);	acobelli,	3):1319-1	t al., J Im	143 (200]	J Biol C	1998), the	h of whic	ated by	entirety.	pe nsed	ese assay	ole (e.g.,	.();	nan T cel	cording t	he SUPT	suspensi	and IL-4	IIs.						
disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	McGuire and Iacobelli, J	Immunol 159(3):1319-1327	(1997); Parra et al., J Immunol	166(4):2437-2443 (2001); and	Butscher et al., J Biol Chem	3(1):552-560 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety.	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC)	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.						
disclo	66:1-1	Malm	216:30	et al.,	85:63	McGu	Immu	(1997)	166(4)	Butscl	3(1):5	conter	herein	refere	cells t	accord	public	throug	Exem	may b	assays	line, w	culture	respon			-			
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example, melanoma (e.g.,	metastatic melanoma), renal	cell carcinoma (e.g., metastatic	renal cell carcinoma),	leukemia, lymphoma (e.g., T	cell lymphoma), and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	A highly preferred indication	includes infection (e.g.,	AIDS, tuberculosis, infections	associated with granulomatous	disease, and osteoporosis,	and/or as described below	under "Infectious Disease"). A	highly preferred indication is	AIDS. Additional highly	preferred indications include	suppression of immune	reactions to transplanted	organs and/or tissues, uveitis,	psoriasis, and tropical spastic	paraparesis. Preferred	indications include blood
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				disorders (e.g., as described
				Activity", "Blood-Related
				Disorders", and/or
				"Cardiovascular Disorders").
				Preferred indications also
				include anemia, pancytopenia,
				leukopenia, thrombocytopenia,
				Hodgkin's disease, acute
				lymphocytic anemia (ALL),
 _				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, granulomatous
				disease, inflammatory bowel
				disease, sepsis, neutropenia,
				neutrophilia, hemophilia,
				hypercoagulation, diabetes
				mellitus, endocarditis,
				meningitis, Lyme Disease,
				asthma and allergy.
HCWKC15	929	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include neoplastic diseases
		through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
		response element in	Site (GAS) response element	and/or as described below
		immune cells (such	are well-known in the art and	under "Hyperproliferative
		as T-cells).	may be used or routinely	Disorders"). Highly preferred
			modified to assess the ability	indications include neoplasms
-			of polypeptides of the	and cancers, such as, for
	_		invention (including antibodies	example, leukemia, lymphoma
			and agonists or antagonists of	(e.g., T cell lymphoma,
			the invention) to regulate	Burkitt's lymphoma, non-

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Hodgkins lymphoma,	Hodgkin"s disease),	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or
STAT transcription factors and	modulate gene expression	involved in a wide variety of	cell functions. Exemplary	assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the SUPT cell line, that	may be used according to these	assays are publicly available	(e.g., through the ATCC).
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					"Cardiovascular Disorders").
					and infection (e.g., viral
					infections, tuberculosis,
					infections associated with
					chronic granulomatosus
					disease and malignant
_		-			osteoporosis, and/or an
					infectious disease as described
					below under "Infectious
					Disease"). An additional
					preferred indication is
					idiopathic pulmonary fibrosis.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
			_		acute lymphocytic anemia
					(ALL), plasmacytomas,
					multiple myeloma, arthritis,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
-					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
_					reactions to transplanted
_					organs and tissues,
					hemophilia, hypercoagulation,
-					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
	HCWKCIS	576	Activation of	Assays for the activation of	Highly preferred indications
			transcription	transcription through the	include blood disorders (e.g.,

	through NFAT	Nuclear Factor of Activated T	as described below under
	response element in	cells (NFAT) response element	"Immune Activity", "Blood-
	immune cells (such	are well-known in the art and	Related Disorders", and/or
	as T-cells).	may be used or routinely	"Cardiovascular Disorders").
		modified to assess the ability	Highly preferred indications
		of polypeptides of the	include autoimmune diseases
		invention (including antibodies	(e.g., rheumatoid arthritis,
		and agonists or antagonists of	systemic lupus erythematosis,
		the invention) to regulate	multiple sclerosis and/or as
		NFAT transcription factors and	described below),
•		modulate expression of genes	immunodeficiencies (e.g., as
		involved in	described below), boosting a T
		immunomodulatory functions.	cell-mediated immune
		Exemplary assays for	response, and suppressing a T
		transcription through the	cell-mediated immune
		NFAT response element that	response. Additional highly
		may be used or routinely	preferred indications include
		modified to test NFAT-	inflammation and
		response element activity of	inflammatory disorders. An
		polypeptides of the invention	additional highly preferred
		(including antibodies and	indication is infection (e.g., an
		agonists or antagonists of the	infectious disease as described
		invention) include assays	below under "Infectious
		disclosed in Berger et al., Gene	Disease"). Preferred
		66:1-10 (1998); Cullen and	indications include neoplastic
		Malm, Methods in Enzymol	diseases (e.g., leukemia,
		216:362-368 (1992); Henthorn	lymphoma, and/or as described
		et al., Proc Natl Acad Sci USA	below under
		85:6342-6346 (1988); Serfling	"Hyperproliferative
		et al., Biochim Biophys Acta	Disorders"). Preferred
		1498(1):1-18 (2000); De Boer	indications include neonlasms

				et al., Int J Biochem Cell Biol	and cancers, such as, for
				31(10):1221-1236 (1999);	example, leukemia, lymphoma,
				Fraser et al., Eur J Immunol	and prostate, breast, lung,
-				29(3):838-844 (1999); and	colon, pancreatic, esophageal,
		_		Yeseen et al., J Biol Chem	stomach, brain, liver and
				268(19):14285-14293 (1993),	urinary cancer. Other preferred
				the contents of each of which	indications include benign
				are herein incorporated by	dysproliferative disorders and
				reference in its entirety. T	pre-neoplastic conditions, such
				cells that may be used	as, for example, hyperplasia,
				according to these assays are	metaplasia, and/or dysplasia.
-				publicly available (e.g.,	Preferred indications also
				through the ATCC).	include anemia, pancytopenia,
				Exemplary human T cells that	leukopenia, thrombocytopenia,
				may be used according to these	Hodgkin's disease, acute
				assays include the SUPT cell	lymphocytic anemia (ALL),
				line, which is a suspension	plasmacytomas, multiple
				culture of IL-2 and IL-4	myeloma, Burkitt's lymphoma,
				responsive T cells.	arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
_					diabetes mellitus, endocarditis,
_					meningitis, Lyme Disease,
					asthma and allergy.
Ĭ.	HCWKC15	216	Activation of	Assays for the activation of	Highly preferred indications
			transcription	transcription through the	include inflammation and

	through NFKB	NFKB response element are	inflammatory disorders.	
	response element in	well-known in the art and may	Highly preferred indications	
	immune cells (such	be used or routinely modified	include blood disorders (e.g.,	-
	as T-cells).	to assess the ability of	as described below under	
		polypeptides of the invention	"Immune Activity", "Blood-	
		(including antibodies and	Related Disorders", and/or	
-		agonists or antagonists of the	"Cardiovascular Disorders").	
		invention) to regulate NFKB	Highly preferred indications	
		transcription factors and	include autoimmune diseases	
		modulate expression of	(e.g., rheumatoid arthritis,	
		immunomodulatory genes.	systemic lupus erythematosis,	
		Exemplary assays for	multiple sclerosis and/or as	
		transcription through the	described below), and	
		NFKB response element that	immunodeficiencies (e.g., as	
		may be used or rountinely	described below). An	
		modified to test NFKB-	additional highly preferred	
		response element activity of	indication is infection (e.g.,	
		polypeptides of the invention	AIDS, and/or an infectious	
		(including antibodies and	disease as described below	
		agonists or antagonists of the	under "Infectious Disease").	
	200-20	invention) include assays	Highly preferred indications	
		disclosed in Berger et al., Gene	include neoplastic diseases	
		66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,	
		Malm, Methods in Enzymol	lymphoma, and/or as described	
-		216:362-368 (1992); Henthorn	below under	
		et al., Proc Natl Acad Sci USA	"Hyperproliferative	
		85:6342-6346 (1988); Black et	Disorders"). Highly preferred	_
		al., Virus Gnes 15(2):105-117	indications include neoplasms	
		(1997); and Fraser et al.,	and cancers, such	
		29(3):838-844 (1999), the	as,melanoma, renal cell	
		contents of each of which are	carcinoma, leukemia,	

			herein incorporated by	lymphoma, and prostate,
 -			reference in its entirety. T	breast, lung, colon, pancreatic,
			cells that may be used	esophageal, stomach, brain,
			according to these assays are	liver and urinary cancer. Other
			publicly available (e.g.,	preferred indications include
			through the ATCC).	benign dysproliferative
			Exemplary human T cells that	disorders and pre-neoplastic
			may be used according to these	conditions, such as, for
			assays include the SUPT cell	example, hyperplasia,
			line, which is a suspension	metaplasia, and/or dysplasia.
			culture of IL-2 and IL-4	Preferred indications also
			responsive T cells.	include anemia, pancytopenia,
				leukopenia, thrombocytopenia,
 				Hodgkin's disease, acute
	-			lymphocytic anemia (ALL),
 				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS,
				granulomatous disease,
 				inflammatory bowel disease,
				sepsis, neutropenia,
				neutrophilia, psoriasis,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
				suppression of immune
				reactions to transplanted
				organs, asthma and allergy.
HCWLD74	577	Activation of	Assays for the activation of	A highly preferred indication
		transcription	transcription through the	is obesity and/or complications
		through cAMP	cAMP response element are	associated with obesity.

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Additional highly preferred indications include weight loss	or alternatively, weight gain.	An additional highly preferred	indication is diabetes mellitus.	An additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as
well-known in the art and may be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to increase cAMP,	regulate CREB transcription	factors, and modulate	expression of genes involved	in a wide variety of cell	functions. For example, a	3T3-L1/CRE reporter assay	may be used to identify factors	that activate the cAMP	signaling pathway. CREB	plays a major role in	adipogenesis, and is involved	in differentiation into	adipocytes. CRE contains the	binding sequence for the	transcription factor CREB	(CRE binding protein).	Exemplary assays for	transcription through the	cAMP response element that	may be used or routinely	modified to test cAMP-	response element activity of	polypeptides of the invention	(including antibodies and
response element (CRE) in pre-	adipocytes.																												
					and a														-							•			
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described in the "Cardiovascular Disorders" section below), dyslipidemia,	endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection	(e.g., infectious diseases and disorders as described in the	infectious Diseases section below, especially of the	urinary tract and skin), carpal tunnel syndrome and	Dupuytren's contracture). Additional highly preferred	indications are complications	resistance.						
agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch et al., Mol Cell Biol 20(3):1008-1020 (2000); and	Klemm et al., J Biol Chem 273:917-923 (1998), the	herein incorporated by	reference in its entirety. Preadipocytes that may be used	according to these assays are publicly available (e.g.,	through the ATCC) and/or may be routinely generated	Exemplary mouse adipocyte	cells that may be used according to these assays	include 3T3-L1 cells. 3T3-L1 is an adherent mouse	preadipocyte cell line that is a	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to adipose-like conversion under
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Activation of This reporter assay measures transcription activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 response element in immune cells (such as mast cells). Activation of GATA-3 in mast cells as mast cells). Cytokine and chemokine production. Assays for the activation of franscription through the GATA3 response element are well-known in the activation of transcription through the GATA3 response element are well-known in the activation of transcription frought the GATA3 transcription from and agonists of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response development. Exemplary assays for transcription through the GATA3 response element that may be used or	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indication (e.g., an infectious disease as described below under "Infectious Disease"), and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia,	
GATA3-response element activity of polypeptides of the	lymphoma, melanoma, prostate, breast, lung, colon, pancreatic, esophageal,	

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urinary tract cancers and/or as described below under "Hyperproliferative Disorders"). Other preferred	indications include benign dysproliferative disorders and	as, for example, hyperplasia, metaplasia, and/or dysplasia.	Preferred indications include anemia nancytonenia	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	mennights, and Lyme Disease.			
and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998): Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al. Proc Natl Acad Sci 118 A	85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999); Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,	unough me AICC).	Exemplary numan mast cells	these seed according to	these assays include the HMC-	immoture human mast and the	established from the peripheral	blood of a patient with mast	cell lenkemia and exhibits
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				many characteristics of	
				immature mast cells.	
HCWLD74	,D74	577	Activation of	This reporter assay measures	Highly preferred indications
			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
-			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
-			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
-				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
			-	response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
-				modulate expression of genes	below) and
				involved in	immunodeficiencies (e.g., as
				immunomodulatory functions.	described below). Preferred
				Exemplary assays for	indications include neoplastic
_				transcription through the	diseases (e.g., leukemia,
	·			NFAT response element that	lymphoma, melanoma,
		,		may be used or routinely	prostate, breast, lung, colon,
				modified to test NFAT-	pancreatic, esophageal,
				response element activity of	stomach, brain, liver, and

				blood of a natient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
HCWLD74	₹	577	Activation of	Assays for the activation of	Preferred indications include
			transcription	transcription through the	blood disorders (e.g., as
			through cAMP	cAMP response element are	described below under
			response element in	well-known in the art and may	"Immune Activity", "Blood-
			immune cells (such	be used or routinely modified	Related Disorders", and/or
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
				(including antibodies and	infectious disease as described
				agonists or antagonists of the	below under "Infectious
				invention) to increase cAMP,	Disease"). Preferred
				regulate CREB transcription	indications include
				factors, and modulate	autoimmune diseases (e.g.,
				expression of genes involved	rheumatoid arthritis, systemic
				in a wide variety of cell	lupus erythematosis, multiple
				functions. Exemplary assays	sclerosis and/or as described
				for transcription through the	below), immunodeficiencies
				cAMP response element that	(e.g., as described below),
				may be used or routinely	boosting a T cell-mediated
				modified to test cAMP-	immune response, and
				response element activity of	suppressing a T cell-mediated
				polypeptides of the invention	immune response. Additional
				(including antibodies and	preferred indications include
				agonists or antagonists of the	inflammation and
				invention) include assays	inflammatory disorders.
				disclosed in Berger et al., Gene	Highly preferred indications
_			_	66:1-10 (1998); Cullen and	include neoplastic diseases
				Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,

	216:362-368 (1992): Henthorn	and/or as described below
	et al., Proc Natl Acad Sci USA	under "Hyperproliferative
	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	al., Virus Genes 15(2):105-117	indications include neoplasms
	(1997); and Belkowski et al., J	and cancers, such as, for
	Immunol 161(2):659-665	example, leukemia, lymphoma
	(1998), the contents of each of	(e.g., T cell lymphoma,
·	which are herein incorporated	Burkitt's lymphoma, non-
	by reference in its entirety. T	Hodgkins lymphoma,
	cells that may be used	Hodgkin"s disease),
	according to these assays are	melanoma, and prostate,
	publicly available (e.g.,	breast, lung, colon, pancreatic,
	through the ATCC).	esophageal, stomach, brain,
	Exemplary mouse T cells that	liver and urinary cancer. Other
	may be used according to these	preferred indications include
	assays include the HT2 cell	benign dysproliferative
	line, which is a suspension	disorders and pre-neoplastic
	culture of IL-2 dependent T	conditions, such as, for
	cells that also respond to IL-4.	example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications include
		anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		acute lymphocytic anemia
		(ALL), plasmacytomas,
		multiple myeloma, arthritis,
		AIDS, granulomatous disease,
	A	inflammatory bowel disease,
		sepsis, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune

			·	reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
HCWLD74	577	Activation of transcription	Assays for the activation of transcription through the	Highly preferred indications include blood disorders (e.g.
		through NFAT	Nuclear Factor of Activated T	as described below under
		response element in	cells (NFAT) response element	"Immune Activity", "Blood-
		immune cells (such	are well-known in the art and	Related Disorders", and/or
		as natural killer	may be used or routinely	"Cardiovascular Disorders").
		cells).	modified to assess the ability	Highly preferred indications
			of polypeptides of the	include autoimmune diseases
			invention (including antibodies	(e.g., rheumatoid arthritis,
			and agonists or antagonists of	systemic lupus erythematosis,
			the invention) to regulate	multiple sclerosis and/or as
			NFAT transcription factors and	described below),
			modulate expression of genes	immunodeficiencies (e.g., as
			involved in	described below), boosting a T
			immunomodulatory functions.	cell-mediated immune
			Exemplary assays for	response, and suppressing a T
			transcription through the	cell-mediated immune
			NFAT response element that	response. Additional highly
			may be used or routinely	preferred indications include
			modified to test NFAT-	inflammation and
			response element activity of	inflammatory disorders. An
			polypeptides of the invention	additional highly preferred
			(including antibodies and	indication is infection (e.g., an
			agonists or antagonists of the	infectious disease as described
			invention) include assays	below under "Infectious

	disclosed in Berger et al Gene	Disease"). Preferred
	66:1-10 (1998); Cullen and	inc
	Malm, Methods in Enzymol	diseases (e.g., leukemia,
	216:362-368 (1992); Henthorn	lymphoma, and/or as described
	et al., Proc Natl Acad Sci USA	below under
	85:6342-6346 (1988);	"Hyperproliferative
	Aramburu et al., J Exp Med	Disorders"). Preferred
	182(3):801-810 (1995); De	indications include neoplasms
	Boer et al., Int J Biochem Cell	and cancers, such as, for
	Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
	Fraser et al., Eur J Immunol	and prostate, breast, lung,
-	29(3):838-844 (1999); and	colon, pancreatic, esophageal,
	Yeseen et al., J Biol Chem	stomach, brain, liver and
	268(19):14285-14293 (1993),	urinary cancer. Other preferred
	the contents of each of which	indications include benign
	are herein incorporated by	dysproliferative disorders and
	reference in its entirety. NK	pre-neoplastic conditions, such
	cells that may be used	as, for example, hyperplasia,
	according to these assays are	metaplasia, and/or dysplasia.
~	publicly available (e.g.,	Preferred indications also
	through the ATCC).	include anemia, pancytopenia,
	Exemplary human NK cells	leukopenia, thrombocytopenia,
	that may be used according to	Hodgkin's disease, acute
	these assays include the NK-	lymphocytic anemia (ALL),
	YT cell line, which is a human	plasmacytomas, multiple
	natural killer cell line with	myeloma, Burkitt's lymphoma,
	cytolytic and cytotoxic	arthritis, AIDS, granulomatous
	activity.	disease, inflammatory bowel
		disease, sepsis, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune

				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
				asthma and allergy.
HCWLD74	577	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as natural killer	routinely modified to assess	highly preferred embodiment
		cells).	the ability of polypeptides of	of the invention includes a
			the invention (including	method for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate serum response	indications include blood
			factors and modulate the	disorders (e.g., as described
			expression of genes involved	below under "Immune
			in growth and upregulate the	Activity", "Blood-Related
			function of growth-related	Disorders", and/or
			genes in many cell types.	"Cardiovascular Disorders"),
			Exemplary assays for	Highly preferred indications
			transcription through the SRE	include autoimmune diseases
			that may be used or routinely	(e.g., rheumatoid arthritis,
			modified to test SRE activity	systemic lupus erythematosis,
			of the polypeptides of the	Crohn"s disease, multiple
			invention (including antibodies	sclerosis and/or as described
			and agonists or antagonists of	below), immunodeficiencies
			the invention) include assays	(e.g., as described below),
			disclosed in Berger et al., Gene	boosting a T cell-mediated

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immune response, and	suppressing a 1 cen-mediated immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia.
66:1-10 (1998); Cullen and Malm Methods in Engagnol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.										
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					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
	-				leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
				_	lymphocytic anemia (ALL),
		-			plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
_					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
		-			organs and tissues, hemophilia,
					hypercoagulation, diabetes
		***			mellitus, endocarditis,
	ma,				meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
_					is infection (e.g., an infectious
					disease as described below
	7 11 11 11 11 11 11 11 11 11 11 11 11 11				under "Infectious Disease").
	HCWLD/4	577	Activation of	Assays for the activation of	Highly preferred indications
			transcription	transcription through the	include neoplastic diseases
			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
			response element in	Site (GAS) response element	and/or as described below
			immune cells (such	are well-known in the art and	under "Hyperproliferative
			as T-cells).	may be used or routinely	Disorders"). Highly preferred
				modified to assess the ability	indications include neoplasms

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and cancers, such as, for example, leukemia, lymphoma	(e.g., T cell lymphoma,	Hodgkins lymphoma,	Hodgkin"s disease),	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications
of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) to regulate	STAT transcription factors and	modulate gene expression	involved in a wide variety of	cell functions. Exemplary	assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,
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include blood disorders (e.g.,		"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, arthritis,	AIDS, granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	dialector mealiters and 1.1.
such as the SUPT cell line, that	may be used according to these	assays are publicly available	(e.g., through the ATCC).																											
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				meningitis, Lyme Disease, and
HDHEB60	578	Activation of	Assays for the activation of	A highly preferred indication
		transcription	transcription through the	is obesity and/or complications
		through cAMP	cAMP response element are	associated with obesity.
		response element	well-known in the art and may	Additional highly preferred
		(CRE) in pre-	be used or routinely modified	indications include weight loss
		adipocytes.	to assess the ability of	or alternatively, weight gain.
			polypeptides of the invention	An additional highly preferred
			(including antibodies and	indication is diabetes mellitus.
			agonists or antagonists of the	An additional highly preferred
	_		invention) to increase cAMP,	indication is a complication
			regulate CREB transcription	associated with diabetes (e.g.,
			factors, and modulate	diabetic retinopathy, diabetic
			expression of genes involved	nephropathy, kidney disease
			in a wide variety of cell	(e.g., renal failure,
			functions. For example, a	nephropathy and/or other
			3T3-L1/CRE reporter assay	diseases and disorders as
			may be used to identify factors	described in the "Renal
			that activate the cAMP	Disorders" section below),
	3-2		signaling pathway. CREB	diabetic neuropathy, nerve
			plays a major role in	disease and nerve damage
			adipogenesis, and is involved	(e.g., due to diabetic
_			in differentiation into	neuropathy), blood vessel
			adipocytes. CRE contains the	blockage, heart disease, stroke,
			binding sequence for the	impotence (e.g., due to diabetic
			transcription factor CREB	neuropathy or blood vessel
			(CRE binding protein).	blockage), seizures, mental
			Exemplary assays for	confusion, drowsiness,
			transcription through the	nonketotic hyperglycemic-
			cAMP response element that	hyperosmolar coma,

 may be used or routinely	cardiovascular disease (e.g.,
modified to test cAMP-	heart disease, atherosclerosis,
response element activity of	microvascular disease,
 polypeptides of the invention	hypertension, stroke, and other
(including antibodies and	diseases and disorders as
agonists or antagonists of the	described in the
invention) include assays	"Cardiovascular Disorders"
disclosed in Berger et al., Gene	section below), dyslipidemia,
 66:1-10 (1998); Cullen and	endocrine disorders (as
 Malm, Methods in Enzymol	described in the "Endocrine
 216:362-368 (1992); Henthorn	Disorders" section below),
et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
et al., Mol Cell Biol	blindness), ulcers and impaired
20(3):1008-1020 (2000); and	wound healing, and infection
 Klemm et al., J Biol Chem	(e.g., infectious diseases and
273:917-923 (1998), the	disorders as described in the
contents of each of which are	"Infectious Diseases" section
herein incorporated by	below, especially of the
reference in its entirety. Pre-	urinary tract and skin), carpal
adipocytes that may be used	tunnel syndrome and
according to these assays are	Dupuytren's contracture).
publicly available (e.g.,	Additional highly preferred
 through the ATCC) and/or	indications are complications
may be routinely generated.	associated with insulin
Exemplary mouse adipocyte	resistance.
 cells that may be used	
according to these assays	
include 3T3-L1 cells. 3T3-L1	
 is an adherent mouse	
preadipocyte cell line that is a	

				continuous substrain of 3T3	
				fibroblast cells developed	
				through clonal isolation and	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
				conditions known in the art.	
HDF	HDHEB60	578	Myoblast cell	Assays for muscle cell	Highly preferred indications
			proliferation	proliferation are well known in	include diabetes, myopathy,
	_			the art and may be used or	muscle cell atrophy, cancers of
				routinely modified to assess	muscle (such as,
				the ability of polypeptides of	rhabdomyoma, and
				the invention (including	rhabdosarcoma),
				antibodies and agonists or	cardiovascular disorders (such
				antagonists of the invention) to	as congestive heart failure,
				stimulate or inhibit myoblast	cachexia, myxomas, fibromas,
				cell proliferation. Exemplary	congenital cardiovascular
				assays for myoblast cell	abnormalities, heart disease,
	-			proliferation that may be used	cardiac arrest, heart valve
				or routinely modified to test	disease, vascular disease, and
				activity of polypeptides and	also as described below under
				antibodies of the invention	"Cardiovascular Disorders"),
				(including agonists or	stimulating myoblast
				antagonists of the invention)	proliferation, and inhibiting
				include, for example, assays	myoblast proliferation.
				disclosed in: Soeta, C., et al.	
-				"Possible role for the c-ski	
				gene in the proliferation of	
				myogenic cells in regenerating	
				skeletal muscles of rats" Dev	
				Growth Differ Apr;43(2):155-	

	Highly preferred indications include inflammation (acute and chronic), restnosis,
64 (2001); Ewton DZ, et al., "IGF binding proteins-4, -5 and -6 may play specialized roles during L6 myoblast proliferation and differentiation." J Endocrinol Mar; 144(3):539-53 (1995); and, Pampusch MS, et al., "Effect of transforming growth factor beta on proliferation of L6 and embryonic porcine myogenic cells." J Cell Physiol Jun; 143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety. Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.	Assays for measuring expression of VCAM are well-known in the art and may be
	Production of VCAM in endothelial cells
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atherosclerosis, asthma and	allergy. Highly preferred	indications include	inflammation and	inflammatory disorders,	immunological disorders,	neoplastic disorders (e.g.	cancer/tumorigenesis), and		as described below under	"Immune Activity", "Blood-	Related Disorders",	"Hyperproliferative Disorders"	and/or "Cardiovascular	Disorders"). Highly preferred		and cancers such as, for	example, leukemia, lymphoma,	melanoma, renal cell	carcinoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	•	
used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate VCAM	expression. For example,	FMAT may be used to meaure	the upregulation of cell surface	VCAM-1 expresssion in	endothelial cells. Endothelial	cells are cells that line blood	vessels, and are involved in	functions that include, but are	not limited to, angiogenesis,	vascular permeability, vascular	tone, and immune cell	extravasation. Exemplary	endothelial cells that may be	used according to these assays	include human umbilical vein	endothelial cells (HUVEC),	which are available from	commercial sources. The	expression of VCAM	(CD106), a membrane-	associated protein, can be	upregulated by cytokines or	other factors, and contributes	to the extravasation of	lymphocytes, leucocytes and
(such as human	umbilical vein	endothelial cells	(HUVEC))								-																			
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	Highly preferred indications	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response. Additional highly	preferred indications include	inflammation and	inflammatory disorders. An	additional highly preferred	indication is infection (e.g., an	infectious disease as described	below under "Infectious	Dispase") Droformod
other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.	Assays for the activation of	Nuclear Factor of Activated T	cells (NFAT) response element	are well-known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to regulate	NFAT transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Rerger et al Gene
	Activation of transcription	through NFAT	response element in	immune cells (such	as natural killer	cells).																			
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	HDHEB60																								
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	66:1-10 (1998): Cullen and	indications include neonlastic
	Malm, Methods in Enzymol	diseases (e.g., leukemia,
	216:362-368 (1992); Henthorn	lymphoma, and/or as described
	et al., Proc Natl Acad Sci USA	below under
	85:6342-6346 (1988);	"Hyperproliferative
	Aramburu et al., J Exp Med	Disorders"). Preferred
	182(3):801-810 (1995); De	indications include neoplasms
	Boer et al., Int J Biochem Cell	and cancers, such as, for
	Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
	Fraser et al., Eur J Immunol	and prostate, breast, lung,
	29(3):838-844 (1999); and	colon, pancreatic, esophageal,
	Yeseen et al., J Biol Chem	stomach, brain, liver and
	268(19):14285-14293 (1993),	urinary cancer. Other preferred
	the contents of each of which	indications include benign
	are herein incorporated by	dysproliferative disorders and
	reference in its entirety. NK	pre-neoplastic conditions, such
	cells that may be used	as, for example, hyperplasia,
	according to these assays are	metaplasia, and/or dysplasia.
	publicly available (e.g.,	Preferred indications also
	through the ATCC).	include anemia, pancytopenia,
	Exemplary human NK cells	leukopenia, thrombocytopenia,
	that may be used according to	Hodgkin's disease, acute
	these assays include the NK-	lymphocytic anemia (ALL),
	YT cell line, which is a human	plasmacytomas, multiple
-	natural killer cell line with	myeloma, Burkitt's lymphoma,
	cytolytic and cytotoxic	arthritis, AIDS, granulomatous
	activity.	disease, inflammatory bowel
		disease, sepsis, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted

					organs and tissues.
-		-			hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
	() datidit				asthma and allergy.
	HDHEB60	578	Activation of	Assays for the activation of	Highly preferred indications
•			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as natural killer	to assess the ability of	as described below under
			cells).	polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
-				transcription through the	described below), and
				NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
	-			invention) include assays	Highly preferred indications
			-	disclosed in Berger et al., Gene	include neoplastic diseases
				66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
				Malm, Methods in Enzymol	lymphoma, and/or as described

		216:362-368 (1992); Henthorn	below under
		et al., Proc Natl Acad Sci USA	"Hyperproliferative
		85:6342-6346 (1988); Valle	Disorders"). Highly preferred
		Blazquez et al, Immunology	indications include neoplasms
		90(3):455-460 (1997);	and cancers, such as, for
		Aramburau et al., J Exp Med	example, melanoma, renal cell
		82(3):801-810 (1995); and	carcinoma, leukemia,
		Fraser et al., 29(3):838-844	lymphoma, and prostate,
		(1999), the contents of each of	breast, lung, colon, pancreatic,
		which are herein incorporated	esophageal, stomach, brain,
		by reference in its entirety.	liver and urinary cancer. Other
		NK cells that may be used	preferred indications include
		according to these assays are	benign dysproliferative
		publicly available (e.g.,	disorders and pre-neoplastic
		through the ATCC).	conditions, such as, for
		Exemplary NK cells that may	example, hyperplasia,
		be used according to these	metaplasia, and/or dysplasia.
		assays include the NK-YT cell	Preferred indications also
		line, which is a human natural	include anemia, pancytopenia,
		killer cell line with cytolytic	leukopenia, thrombocytopenia,
		and cytotoxic activity.	Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
-			disease, inflammatory bowel
-			disease, sepsis, neutropenia,
			neutrophilia, psoriasis,
			hemophilia, hypercoagulation,
			diabetes mellitus, endocarditis,
			meningitis, Lyme Disease,

			Chang et al., Mol Cell Biol	below under
			18(9):4986-4993 (1998); and	"Hyperproliferative
			Fraser et al., Eur J Immunol	Disorders"). Highly preferred
			29(3):838-844 (1999), the	indications include neoplasms
			contents of each of which are	and cancers, such as, leukemia,
			herein incorporated by	lymphoma, prostate, breast,
			reference in its entirety.	lung, colon, pancreatic,
-			Human T cells that may be	esophageal, stomach, brain,
			used according to these assays	liver, and urinary cancer. Other
-			are publicly available (e.g.,	preferred indications include
-			through the ATCC).	benign dysproliferative
			Exemplary human T cells that	disorders and pre-neoplastic
			may be used according to these	conditions, such as, for
	-		assays include the SUPT cell	example, hyperplasia,
			line, which is an IL-2 and IL-4	metaplasia, and/or dysplasia.
			responsive suspension-culture	Preferred indications include
			cell line.	arthritis, asthma, AIDS,
				allergy, anemia, pancytopenia,
				leukopenia, thrombocytopenia,
				Hodgkin's disease, acute
			-	Iymphocytic anemia (ALL),
				plasmacytomas, multiple
		1,5-	-	myeloma, Burkitt's lymphoma,
				granulomatous disease,
				inflammatory bowel disease,
				sepsis, psoriasis, suppression of
		_		immune reactions to
				transplanted organs and
				tissues, endocarditis,
				meningitis, and Lyme Disease.
HDHEB60	578	Activation of	Assays for the activation of	A highly preferred

transcription	transcription through the CD28 embodiment of the invention	embodiment of the invention
through CD28	response element are well-	includes a method for
response element in	known in the art and may be	stimulating T cell proliferation.
immune cells (such	used or routinely modified to	An alternative highly preferred
as T-cells).	assess the ability of	embodiment of the invention
	polypeptides of the invention	includes a method for
	(including antibodies and	inhibiting T cell proliferation.
	agonists or antagonists of the	A highly preferred
	invention) to stimulate IL-2	embodiment of the invention
	expression in T cells.	includes a method for
	Exemplary assays for	activating T cells. An
	transcription through the CD28	alternative highly preferred
	response element that may be	embodiment of the invention
	used or routinely modified to	includes a method for
	test CD28-response element	inhibiting the activation of
	activity of polypeptides of the	and/or inactivating T cells.
	invention (including antibodies	A highly preferred
	and agonists or antagonists of	embodiment of the invention
	the invention) include assays	includes a method for
	disclosed in Berger et al., Gene	stimulating (e.g., increasing)
	66:1-10 (1998); Cullen and	IL-2 production. An alternative
	Malm, Methods in Enzymol	highly preferred embodiment
-	216:362-368 (1992); Henthorn	of the invention includes a
	et al., Proc Natl Acad Sci USA	method for inhibiting (e.g.,
	85:6342-6346 (1988);	reducing) IL-2 production.
	McGuire and Iacobelli, J	Additional highly preferred
	Immunol 159(3):1319-1327	indications include
	(1997); Parra et al., J Immunol	inflammation and
	166(4):2437-2443 (2001); and	inflammatory disorders.
	Butscher et al., J Biol Chem	Highly preferred indications
	3(1):552-560 (1998), the	include autoimmune diseases

contents of each of which are	(e.g., rheumatoid arthritis,
herein incorporated by	systemic lupus erythematosis,
reference in its entirety. T	multiple sclerosis and/or as
cells that may be used	described below),
according to these assays are	immunodeficiencies (e.g., as
publicly available (e.g.,	described below), boosting a T
through the ATCC).	cell-mediated immune
Exemplary human T cells that	response, and suppressing a T
may be used according to these	
assays include the SUPT cell	response. Highly preferred
line, which is a suspension	indications include neoplastic
culture of IL-2 and IL-4	diseases (e.g., melanoma, renal
responsive T cells.	cell carcinoma, leukemia,
	lymphoma, and/or as described
	below under
	"Hyperproliferative
	Disorders"). Highly preferred
	indications include neoplasms
	and cancers, such as, for
	example, melanoma (e.g.,
	metastatic melanoma), renal
	cell carcinoma (e.g., metastatic
	renal cell carcinoma),
	leukemia, lymphoma (e.g., T
	cell lymphoma), and prostate,
	breast, lung, colon, pancreatic,
	esophageal, stomach, brain,
	liver and urinary cancer. Other
	preferred indications include
	benign dysproliferative
	disorders and pre-neoplastic

conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	A highly preferred indication	includes infection (e.g.,	AIDS, tuberculosis, infections	associated with granulomatous	disease, and osteoporosis,	and/or as described below	under "Infectious Disease"). A	highly preferred indication is	AIDS. Additional highly	preferred indications include	suppression of immune	reactions to transplanted	organs and/or tissues, uveitis,	paraparesis. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	mveloma Burkitt's lymnhoma
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										-																			

				arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
nDhebou	8/C	Acuvation of transcription through GAS response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma,
			modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of	Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.

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Preferred indications include autoimmune diseases (e.g.,	rheumatoid arthritis, systemic lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a 1 cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	preferred indication is
the invention) include assays disclosed in Berger et al., Gene	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	132(0):1360-1391 (1399); and Henttinen et el Trummel	renumen et al., Jimmunol	155(10):4582-458/ (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the SUPT cell line, that	may be used according to these	assays are publicly available	(e.g., through the ATCC).											
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immunomodulatory functions.	cell-mediated immune
Exemplary assays for	response, and suppressing a T
transcription through the	cell-mediated immune
NFAT response element that	response. Additional highly
may be used or routinely	preferred indications include
modified to test NFAT-	inflammation and
 response element activity of	inflammatory disorders. An
 polypeptides of the invention	additional highly preferred
 (including antibodies and	indication is infection (e.g., an
agonists or antagonists of the	infectious disease as described
invention) include assays	below under "Infectious
disclosed in Berger et al., Gene	Disease"). Preferred
66:1-10 (1998); Cullen and	indications include neoplastic
Malm, Methods in Enzymol	diseases (e.g., leukemia,
 216:362-368 (1992); Henthorn	lymphoma, and/or as described
et al., Proc Natl Acad Sci USA	below under
 85:6342-6346 (1988); Serfling	"Hyperproliferative
et al., Biochim Biophys Acta	Disorders"). Preferred
1498(1):1-18 (2000); De Boer	indications include neoplasms
et al., Int J Biochem Cell Biol	and cancers, such as, for
31(10):1221-1236 (1999);	example, leukemia, lymphoma,
Fraser et al., Eur J Immunol	and prostate, breast, lung,
29(3):838-844 (1999); and	colon, pancreatic, esophageal,
Yeseen et al., J Biol Chem	stomach, brain, liver and
268(19):14285-14293 (1993),	urinary cancer. Other preferred
the contents of each of which	indications include benign
 are herein incorporated by	dysproliferative disorders and
reference in its entirety. T	pre-neoplastic conditions, such
cells that may be used	as, for example, hyperplasia,
according to these assays are	metaplasia, and/or dysplasia.
publicly available (e.g.,	Preferred indications also

			through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
HDHEB60	578	Activation of transcription through NFKB response element in immune cells (such as T-cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as

	- 14 of a constant and the second	1-1-1-1
	transcription inrough the	described below), and
	NFKB response element that	immunodeficiencies (e.g., as
	may be used or rountinely	described below). An
	modified to test NFKB-	additional highly preferred
	response element activity of	indication is infection (e.g.,
	polypeptides of the invention	AIDS, and/or an infectious
	(including antibodies and	disease as described below
	agonists or antagonists of the	under "Infectious Disease").
	invention) include assays	Highly preferred indications
	disclosed in Berger et al., Gene	include neoplastic diseases
	66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
	Malm, Methods in Enzymol	lymphoma, and/or as described
	216:362-368 (1992); Henthorn	below under
	et al., Proc Natl Acad Sci USA	"Hyperproliferative
	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	al., Virus Gnes 15(2):105-117	indications include neoplasms
	(1997); and Fraser et al.,	and cancers, such
	29(3):838-844 (1999), the	as, melanoma, renal cell
	contents of each of which are	carcinoma, leukemia,
	herein incorporated by	lymphoma, and prostate,
-	reference in its entirety. T	breast, lung, colon, pancreatic,
	cells that may be used	esophageal, stomach, brain,
	according to these assays are	liver and urinary cancer. Other
	publicly available (e.g.,	preferred indications include
	through the ATCC).	benign dysproliferative
	Exemplary human T cells that	disorders and pre-neoplastic
	may be used according to these	conditions, such as, for
	assays include the SUPT cell	example, hyperplasia,
	line, which is a suspension	metaplasia, and/or dysplasia.
	culture of IL-2 and IL-4	Preferred indications also
	responsive T cells.	include anemia, pancytopenia,

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leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted	A highly preferred indication is allergy. Another highly preferred indication is asthma. Additional highly preferred indications include inflammation and inflammation and inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").
	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary
	Activation of transcription through STAT6 response element in immune cells (such as T-cells).
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assays for transcription	autoimmune diseases (e.g.,
through the STAT6 response	rheumatoid arthritis, systemic
element that may be used or	lupus erythematosis, multiple
routinely modified to test	sclerosis and/or as described
 STAT6 response element	below) and
activity of the polypeptides of	immunodeficiencies (e.g., as
the invention (including	described below).
antibodies and agonists or	Preferred indications include
antagonists of the invention)	neoplastic diseases (e.g.,
include assays disclosed in	leukemia, lymphoma,
 Berger et al., Gene 66:1-10	melanoma, and/or as described
 (1998); Cullen and Malm,	below under
 Methods in Enzymol 216:362-	"Hyperproliferative
 368 (1992); Henthorn et al.,	Disorders"). Preferred
 Proc Natl Acad Sci USA	indications include neoplasms
 85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
 (1998); Moffatt et al.,	prostate, breast, lung, colon,
 Transplantation 69(7):1521-	pancreatic, esophageal,
1523 (2000); Curiel et al., Eur	stomach, brain, liver and
J Immunol 27(8):1982-1987	urinary cancer. Other preferred
(1997); and Masuda et al., J	indications include benign
 Biol Chem 275(38):29331-	dysproliferative disorders and
 29337 (2000), the contents of	pre-neoplastic conditions, such
each of which are herein	as, for example, hyperplasia,
incorporated by reference in its	metaplasia, and/or dysplasia.
entirety. T cells that may be	Preferred indications include
used according to these assays	anemia, pancytopenia,
are publicly available (e.g.,	leukopenia, thrombocytopenia,
through the ATCC).	Hodgkin's disease, acute
Exemplary T cells that may be	lymphocytic anemia (ALL),

			used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious
HDLAC10	579	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related

Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn's disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,
for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.	
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melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An
			_																											

				additional preferred indication is infection (e.g., an infectious disease as described below
HDLAC10	579	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC).	under "Infectious Disease"). Highly preferred indications include inflammation (acute and chronic), restnosis, athma and allergy. Highly preferred indications include inflammation and inflammation and inflammation and cancer/tumorigenesis), and cardiovascular disorders (e.g. cancer/tumorigenesis), and cardiovascular disorders (such as described below under "Immune Activity", "Blood-Related Disorders", "Hyperproliferative Disorders" and/or "Cardiovascular Disorders"). Highly preferred indications include neoplasms and cancers such as, for example, leukemia, lymphoma, melanoma, renal cell carcinoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach. brain.
			which are available from commercial sources. The	liver and urinary cancer. Other preferred indications include

				expression of VCAM	benign dysproliferative
				(CD106), a membrane-	disorders and pre-neoplastic
				associated protein, can be	conditions, such as, for
				upregulated by cytokines or	example, hyperplasia,
				other factors, and contributes	metaplasia, and/or dysplasia.
				to the extravasation of	
				lymphocytes, leucocytes and	
				other immune cells from blood	
				vessels; thus VCAM	
				expression plays a role in	
_				promoting immune and	
				inflammatory responses.	
	HDPBA28	580	Stimulation of	Assays for measuring secretion	A highly preferred
			insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
			from pancreatic	the art and may be used or	An additional highly preferred
			beta cells.	routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
				Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
				upregulated by glucose and	(e.g., due to diabetic
	_			also by certain	neuropathy), blood vessel
_				proteins/peptides, and	blockage, heart disease, stroke,
·				disregulation is a key	impotence (e.g., due to diabetic
				component in diabetes.	neuropathy or blood vessel

	Exemplary assays that may be	blockage) seizures mental
	used or routinely modified to	confusion, drowsiness,
	test for stimulation of insulin	nonketotic hyperglycemic-
	secretion (from pancreatic	hyperosmolar coma,
	cells) by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Ahren, B., et al.,	diseases and disorders as
	Am J Physiol, 277(4 Pt	described in the
	2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
	al., Endocrinology,	section below), dyslipidemia,
	138(9):3735-40 (1997); Kim,	endocrine disorders (as
	K.H., et al., FEBS Lett,	described in the "Endocrine
	377(2):237-9 (1995); and,	Disorders" section below),
	Miraglia S et. al., Journal of	neuropathy, vision impairment
-	Biomolecular Screening,	(e.g., diabetic retinopathy and
	4:193-204 (1999), the contents	blindness), ulcers and impaired
	of each of which is herein	wound healing, and infection
	incorporated by reference in its	(e.g., infectious diseases and
	entirety. Pancreatic cells that	disorders as described in the
	may be used according to these	"Infectious Diseases" section
	assays are publicly available	below, especially of the
	(e.g., through the ATCC)	urinary tract and skin), carpal
	and/or may be routinely	tunnel syndrome and
	generated. Exemplary	Dupuytren's contracture).
	pancreatic cells that may be	An additional highly preferred
	used according to these assays	indication is obesity and/or
	include rat INS-1 cells. INS-1	complications associated with
	cells are a semi-adherent cell	obesity. Additional highly
	line established from cells	preferred indications include

d weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	Highly preferred indications include allergy and asthma. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response.
isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to assess the ability of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) to modulate IL-10 production and/or T-cell proliferation include, for example, assays such as disclosed and/or cited in.
	Production of IL-10 and activation of T-cells.
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Robinson, DS, et al., "Th-2	cytokines in allergic disease"	Br Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the	contents of each of which are	herein incorporated by	reference in their entirety.	Exemplary cells that may be	used according to these assays	include Th2 cells. IL10	secreted from Th2 cells may be	measured as a marker of Th2	cell activation. Th2 cells are	a class of T cells that secrete	IL4, IL10, IL13, IL5 and IL6.	Factors that induce	differentiation and activation	of Th2 cells play a major role	in the initiation and	pathogenesis of allergy and	asthma. Primary Thelper 2	cells are generated via in vitro	culture under Th2 polarizing	conditions using peripheral	blood lymphocytes isolated	from cord blood.	Assays for the regulation (i.e.
							_																							Regulation of
																														HDPBQ71 581
											-							-												HDP

viability or	increases or decreases) of	include eosinonhilia asthma
proliferation of	viability and proliferation of	allergy, hypersensitivity
immune cells (such	cells in vitro are well-known in	reactions, inflammation, and
as human	the art and may be used or	inflammatory disorders.
 eosinophil EOL-1	routinely modified to assess	Additional highly preferred
cells).	the ability of polypeptides of	indications include immune
	the invention (including	and hematopoietic disorders
	antibodies and agonists or	(e.g., as described below under
	antagonists of the invention) to	"Immune Activity", and
	regulate viability and	"Blood-Related Disorders"),
	proliferation of eosinophil cells	autoimmune diseases (e.g.,
	and cell lines. For example,	rheumatoid arthritis, systemic
	the CellTiter-Gloô	lupus erythematosis, Crohn"s
	Luminescent Cell Viability	disease, multiple sclerosis
	Assay (Promega Corp.,	and/or as described below),
	Madison, WI, USA) can be	immunodeficiencies (e.g., as
	used to measure the number of	described below). Highly
	viable cells in culture based on	preferred indications also
	quantitation of the ATP	include boosting or inhibiting
	present which signals the	immune cell proliferation.
	presence of metabolically	Preferred indications include
	active cells. Eosinophils are a	neoplastic diseases (e.g.,
-	type of immune cell important	leukemia, lymphoma, and/or as
	in allergic responses; they are	described below under
	recruited to tissues and	"Hyperproliferative
	mediate the inflammtory	Disorders"). Highly preferred
	response of late stage allergic	indications include boosting an
	reaction. Eosinophil cell lines	eosinophil-mediated immune
	that may be used according to	response, and suppressing an
	these assays are publicly	eosinophil-mediated immune
	available and/or may be	response.

				routinely generated. Exemplary eosinophil cells that may be used according to these assays include EOL-1 Cells.	
	НБРВQ71	581	Production of IFNgamma using a	IFNgamma FMAT. IFNg plays a central role in the immune	A highly preferred embodiment of the invention
			T cells	system and is considered to be	includes a method for
				a profittiallitiatory cytoxilie. IFNg promotes TH1 and	IFNg. An alternative highly
				inhibits TH2 differentiation;	preferred embodiment of the
		-		promotes IgGZa and inhibits loF secretion: induces	invention includes a method for inhihiting the production of
				macrophage activation; and	IFNg. Highly preferred
				increases MHC expression.	ns
				Assays for immunomodulatory	disorders (e.g., as described
				proteins produced by T cells	below under "Immune
				and NK cells that regulate a	Activity", "Blood-Related
				variety of inflammatory	Disorders", and/or
-				activities and inhibit TH2	"Cardiovascular Disorders"),
				helper cell functions are well	and infection (e.g., viral
				known in the art and may be	infections, tuberculosis,
				used or routinely modified to	infections associated with
				assess the ability of	chronic granulomatosus
				polypeptides of the invention	disease and malignant
				(including antibodies and	osteoporosis, and/or as
				agonists or antagonists of the	described below under
				invention) to mediate	"Infectious Disease"). Highly
				immunomodulation, regulate	preferred indications include
				inflammatory activities,	autoimmune disease (e.g.,
i				modulate TH2 helper cell	rheumatoid arthritis, systemic

		function, and/or mediate	lupus ervthematosis. multiple
		humoral or cell-mediated	sclerosis and/or as described
		immunity. Exemplary assays	below), immunodeficiency
		that test for	(e.g., as described below),
	_	immunomodulatory proteins	boosting a T cell-mediated
		evaluate the production of	immune response, and
		cytokines, such as Interferon	suppressing a T cell-mediated
		gamma (IFNg), and the	immune response. Additional
		activation of T cells. Such	highly preferred indications
		assays that may be used or	include inflammation and
		routinely modified to test	inflammatory disorders.
		immunomodulatory activity of	Additional preferred
		polypeptides of the invention	indications include idiopathic
		(including antibodies and	pulmonary fibrosis. Highly
		agonists or antagonists of the	preferred indications include
		invention) include the assays	neoplastic diseases (e.g.,
		disclosed in Miraglia et al., J	leukemia, lymphoma,
		Biomolecular Screening 4:193-	melanoma, and/or as described
		204 (1999); Rowland et al.,	below under
		"Lymphocytes: a practical	"Hyperproliferative
		approach" Chapter 6:138-160	Disorders"). Highly preferred
		(2000); Gonzalez et al., J Clin	indications include neoplasms
		Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
		Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
-		Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
		et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
		15:749-795 (1997), and	esophageal, stomach, brain,
		Rheumatology (Oxford)	liver and urinary cancer. Other
		38(3):214-20 (1999), the	preferred indications include
		contents of each of which are	benign dysproliferative
		herein incorporated by	disorders and pre-neoplastic

			reference in its entirety.	conditions, such as, for
			Human T cells that may be	example, hyperplasia,
-			used according to these assays	metaplasia, and/or dysplasia.
			may be isolated using	Preferred indications include
			techniques disclosed herein or	anemia, pancytopenia,
			otherwise known in the art.	leukopenia, thrombocytopenia,
			Human T cells are primary	Hodgkin's disease, acute
		-	human lymphocytes that	lymphocytic anemia (ALL),
			mature in the thymus and	plasmacytomas, multiple
			express a T Cell receptor and	myeloma, Burkitt's lymphoma,
			CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
_			cells mediate humoral or cell-	disease, inflammatory bowel
			mediated immunity and may	disease, sepsis, neutropenia,
			be preactivated to enhance	neutrophilia, psoriasis,
			responsiveness to	suppression of immune
			immunomodulatory factors.	reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
				asthma and allergy.
HDPCL63	582	Regulation of	Assays for the regulation of	A highly preferred
		transcription	transcription through the FAS	indication is diabetes mellitus.
		through the FAS	promoter element are well-	An additional highly preferred
		promoter element	known in the art and may be	indication is a complication
		in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
			assess the ability of	diabetic retinopathy, diabetic
			polypeptides of the invention	nephropathy, kidney disease
-	_		(including antibodies and	(e.g., renal failure,
			agonists or antagonists of the	nephropathy and/or other
			invention) to activate the FAS	diseases and disorders as

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described in the "Renal Disorders" section below),	disease and nerve damage	(e.g., due to diabetic	neuropainy), oroog vesser blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section
promoter element in a reporter construct and to regulate transcription of FAS a key	enzyme for lipogenesis. FAS	promoter is regulated by many	SREBP. Insulin increases FAS	gene transcription in livers of	diabetic mice. This	stimulation of transcription is	also somewhat glucose	dependent. Exemplary assays	that may be used or routinely	modified to test for FAS	promoter element activity (in	hepatocytes) by polypeptides	of the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Xiong, S., et al., Proc Natl	Acad Sci U.S.A., 97(8):3948-	53 (2000); Roder, K., et al.,	Eur J Biochem, 260(3):743-51	(1999); Oskouian B, et al.,	Biochem J, 317 (Pt 1):257-65	(1996); Berger, et al., Gene	66:1-10 (1988); and, Cullen,	B., et al., Methods in Enzymol.	216:362–368 (1992), the	contents of each of which is
								-																			
															_												

			herein incorporated by	helow especially of the
			reference in its entirety.	urinary tract and skin) carnal
			Honotocytes that may be used	trimed from doctors and
			richarocytes that may be used	tunnel syndrome and
			according to these assays, such	Dupuytren's contracture).
			as H4IIE cells, are publicly	An additional highly preferred
			available (e.g., through the	indication is obesity and/or
			ATCC) and/or may be	complications associated with
	<u> </u>		routinely generated.	obesity. Additional highly
			Exemplary hepatocytes that	preferred indications include
			may be used according to these	weight loss or alternatively,
			assays include rat liver	weight gain. Aditional
			hepatoma cell line(s) inducible	highly preferred indications are
			with glucocorticoids, insulin,	complications associated with
			or cAMP derivatives.	insulin resistance.
HDPC025	583	Regulation of	Assays for the regulation of	A highly preferred indication
		viability and	viability and proliferation of	is diabetes mellitus. An
		proliferation of	cells in vitro are well-known in	additional highly preferred
		pancreatic beta	the art and may be used or	indication is a complication
		cells.	routinely modified to assess	associated with diabetes (e.g.,
			the ability of polypeptides of	diabetic retinopathy, diabetic
			the invention (including	nephropathy, kidney disease
			antibodies and agonists or	(e.g., renal failure,
			antagonists of the invention) to	nephropathy and/or other
			regulate viability and	diseases and disorders as
			proliferation of pancreatic beta	described in the "Renal
			cells. For example, the Cell	Disorders" section below),
			Titer-Glo luminescent cell	diabetic neuropathy, nerve
			viability assay measures the	disease and nerve damage
			number of viable cells in	(e.g., due to diabetic
			culture based on quantitation	neuropathy), blood vessel
			of the ATP present which	blockage, heart disease, stroke,

	signals the presence of	impotence (e.g., due to diahetic
	metabolically active cells.	neuropathy or blood vessel
	Exemplary assays that may be	blockage) seizures mental
	used or routinely modified to	confusion drowsiness
	test regulation of violitity and	contratori, diowenices,
	test regulation of viability and	nonketotic nypergrycemic-
	proliferation of pancreatic beta	hyperosmolar coma,
	cells by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Ohtani KI, et al.,	diseases and disorders as
	Endocrinology, 139(1):172-8	described in the
	(1998); Krautheim A, et al,	"Cardiovascular Disorders"
	Exp Clin Endocrinol Diabetes,	section below), dyslipidemia,
	107 (1):29-34 (1999), the	endocrine disorders (as
	contents of each of which is	described in the "Endocrine
	herein incorporated by	Disorders" section below),
	reference in its entirety.	neuropathy, vision impairment
	Pancreatic cells that may be	(e.g., diabetic retinopathy and
	used according to these assays	blindness), ulcers and impaired
	are publicly available (e.g.,	wound healing, and infection
-	through the ATCC) and/or	(e.g., infectious diseases and
	may be routinely generated.	disorders as described in the
	Exemplary pancreatic cells that	"Infectious Diseases" section
	may be used according to these	below, especially of the
	assays include HITT15 Cells.	urinary tract and skin), carpal
	HITT15 are an adherent	tunnel syndrome and
	epithelial cell line established	Dupuytren's contracture). An
	from Syrian hamster islet cells	additional highly preferred
	transformed with SV40. These	indication is obesity and/or
	cells express glucagon,	complications associated with

			somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219:	obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
HDPC025	583	Activation of transcription through NFKB response element in	Natl. Acad. Sci. USA 78: 4339-4343, 1981. Assays for the activation of transcription through the NFKB response element are well-known in the art and may	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications
		as T-cells).	be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and	include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases
			modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of	(e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred indication is infection (e.g.,

		polypeptides of the invention	AIDS, and/or an infectious
		(including antibodies and	disease as described below
		agonists or antagonists of the	under "Infectious Disease").
		invention) include assays	Highly preferred indications
		disclosed in Berger et al., Gene	include neoplastic diseases
		66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
		Malm, Methods in Enzymol	lymphoma, and/or as described
		216:362-368 (1992); Henthorn	below under
	-	et al., Proc Natl Acad Sci USA	"Hyperproliferative
-		85:6342-6346 (1988); Black et	Disorders"). Highly preferred
		al., Virus Gnes 15(2):105-117	indications include neoplasms
		(1997); and Fraser et al.,	and cancers, such
		29(3):838-844 (1999), the	as,melanoma, renal cell
		contents of each of which are	carcinoma, leukemia,
-		herein incorporated by	lymphoma, and prostate,
		reference in its entirety. T	breast, lung, colon, pancreatic,
		cells that may be used	esophageal, stomach, brain,
		according to these assays are	liver and urinary cancer. Other
		publicly available (e.g.,	preferred indications include
		through the ATCC).	benign dysproliferative
		Exemplary human T cells that	disorders and pre-neoplastic
		may be used according to these	conditions, such as, for
		assays include the SUPT cell	example, hyperplasia,
		line, which is a suspension	metaplasia, and/or dysplasia.
		culture of IL-2 and IL-4	Preferred indications also
		responsive T cells.	include anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma. Burkitt's lymphoma

					arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					hemophilia, hypercoagulation,
		_			diabetes mellitus, endocarditis,
_					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
	Connecti				organs, asthma and allergy.
	HDPFF39	584	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
			Signaling Pathway.	transduction that regulate cell	described below under
				proliferation, activation, or	"Hyperproliferative
				apoptosis are well known in	Disorders"), blood disorders
				the art and may be used or	(e.g., as described below under
				routinely modified to assess	"Immune Activity",
				the ability of polypeptides of	"Cardiovascular Disorders",
				the invention (including	and/or "Blood-Related
				antibodies and agonists or	Disorders"), and infection
				antagonists of the invention) to	(e.g., an infectious disease as
				promote or inhibit immune cell	described below under
				(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
				activation, and apoptosis.	preferred indications include
				Exemplary assays for JNK and	autoimmune diseases (e.g.,
				p38 kinase activity that may be	rheumatoid arthritis, systemic
		-		used or routinely modified to	lupus erythematosis, multiple
				test JNK and p38 kinase-	sclerosis and/or as described
				induced activity of	below) and
				polypeptides of the invention	immunodeficiencies (e.g., as

		(including antibodies and	described below). Additional
		agonists or antagonists of the	highly preferred indications
		invention) include the assays	include inflammation and
		disclosed in Forrer et al., Biol	inflammatory disorders.
		Chem 379(8-9):1101-1110	Highly preferred indications
		(1998); Gupta et al., Exp Cell	also include neoplastic
		Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
		Kyriakis JM, Biochem Soc	lymphoma, and/or as described
		Symp 64:29-48 (1999); Chang	below under
		and Karin, Nature	"Hyperproliferative
		410(6824):37-40 (2001); and	Disorders"). Highly preferred
-		Cobb MH, Prog Biophys Mol	indications include neoplasms
		Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
		the contents of each of which	lymphoma, prostate, breast,
		are herein incorporated by	lung, colon, pancreatic,
		reference in its entirety. T	esophageal, stomach, brain,
		cells that may be used	liver, and urinary cancer. Other
		according to these assays are	preferred indications include
		publicly available (e.g.,	benign dysproliferative
		through the ATCC).	disorders and pre-neoplastic
		Exemplary mouse T cells that	conditions, such as, for
		may be used according to these	example, hyperplasia,
		assays include the CTLL cell	metaplasia, and/or dysplasia.
		line, which is an IL-2	Preferred indications include
		dependent suspension-culture	arthritis, asthma, AIDS,
		cell line with cytotoxic	allergy, anemia, pancytopenia,
		activity.	leukopenia, thrombocytopenia,
			Hodgkin"s disease, acute
	•		lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt"s lymphoma,

				granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
HDPFF39	584	Inhibition of squalene synthetase gene transcription.	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	
HDPFP29	585	Myoblast cell proliferation	Assays for muscle cell proliferation are well known in the art and may be used or	Highly preferred indications include diabetes, myopathy, muscle cell atrophy, cancers of

		routinely modified to assess	se dons) alosium
		$10^{44} = 1.11^{44} = 6 = 1 - 1.11 = -2$	diabore (sections)
		the ability of polypeptides of	rnaodomyoma, and
		the invention (including	rhabdosarcoma),
		antibodies and agonists or	cardiovascular disorders (such
		antagonists of the invention) to	as congestive heart failure,
		stimulate or inhibit myoblast	cachexia, myxomas, fibromas,
		cell proliferation. Exemplary	congenital cardiovascular
		assays for myoblast cell	abnormalities, heart disease,
		proliferation that may be used	cardiac arrest, heart valve
-		or routinely modified to test	disease, vascular disease, and
		activity of polypeptides and	also as described below under
		antibodies of the invention	"Cardiovascular Disorders"),
		(including agonists or	stimulating myoblast
		antagonists of the invention)	proliferation, and inhibiting
		include, for example, assays	myoblast proliferation.
		disclosed in: Soeta, C., et al.	
		"Possible role for the c-ski	
		gene in the proliferation of	
		myogenic cells in regenerating	
		skeletal muscles of rats" Dev	
		Growth Differ Apr;43(2):155-	
		64 (2001); Ewton DZ, et al.,	
		"IGF binding proteins-4, -5	
		and -6 may play specialized	
		roles during L6 myoblast	
		proliferation and	
	-	differentiation" J Endocrinol	
		Mar;144(3):539-53 (1995);	
		and, Pampusch MS, et	
		al., "Effect of transforming	
		growth factor beta on	

				nucliforntion of 1 6 and	
				promotation of to and	
		··-		emoryonic porcine myogenic	
				cells" J Cell Physiol	
				Jun;143(3):524-8 (1990); the	
_			1.0	contents of each of which are	
				herein incorporated by	
				reference in their entirety.	
				Exemplary myoblast cells that	
				may be used according to these	
				assays include the rat myoblast	
				L6 cell line. Rat myoblast L6	
				cells are an adherent rat	
				myoblast cell line, isolated	
				from primary cultures of rat	
				thigh muscle, that fuse to form	
				multinucleated myotubes and	
				striated fibers after culture in	,
				differentiation media.	
	HDPGI49	586	Activation of	Kinase assay. JNK and p38	A highly preferred
			Endothelial Cell	kinase assays for signal	embodiment of the invention
			p38 or JNK	transduction that regulate cell	includes a method for
			Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
				apoptosis are well known in	growth. An alternative highly
				the art and may be used or	preferred embodiment of the
				routinely modified to assess	invention includes a method
				the ability of polypeptides of	for inhibiting endothelial cell
				the invention (including	growth. A highly preferred
				antibodies and agonists or	embodiment of the invention
				antagonists of the invention) to	includes a method for
				promote or inhibit cell	stimulating endothelial cell
				proliferation, activation, and	proliferation. An alternative

apoptosis. Exemplary assays	highly preferred embodiment
for JNK and p38 kinase	of the invention includes a
activity that may be used or	method for inhibiting
routinely modified to test JNK	endothelial cell proliferation.
and p38 kinase-induced	A highly preferred
 activity of polypeptides of the	embodiment of the invention
invention (including antibodies	includes a method for
and agonists or antagonists of	stimulating apoptosis of
the invention) include the	endothelial cells. An
assays disclosed in Forrer et	alternative highly preferred
al., Biol Chem 379(8-9):1101-	embodiment of the invention
1110 (1998); Gupta et al., Exp	includes a method for
Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
Soc Symp 64:29-48 (1999);	A highly preferred
 Chang and Karin, Nature	embodiment of the invention
410(6824):37-40 (2001); and	includes a method for
Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
the contents of each of which	alternative highly preferred
are herein incorporated by	embodiment of the invention
 reference in its entirety.	includes a method for
Endothelial cells that may be	inhibiting (e.g., decreasing) the
used according to these assays	activation of and/or
are publicly available (e.g.,	inactivating endothelial cells.
through the ATCC).	A highly preferred
Exemplary endothelial cells	embodiment of the invention
that may be used according to	includes a method for
these assays include human	stimulating angiogenisis. An
umbilical vein endothelial cells	alternative highly preferred
(HUVEC), which are	embodiment of the invention

_																														
includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications
endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.	78																							
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Highly	So	κ,	prostate, breast, lung, colon,	_	nd	p	ign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	tions	ease,		hypertension, coronary artery		r.c		ns,		th as				as	ase,		20	
ma. F	preferred indications also	include cancers such as,	ung, c	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	isorde	nditio	yperp	r dysp	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	onary	itory	vasculitides, Reynaud"s	s,pna	phenomenom, aneurysms,	and	lymphatic disorders such as			lymphedema; and other	vascular disorders such as	peripheral vascular disease,	Highly	preferred indications also	ch as
sarco	dicati	cers s	east, l	esoph	rain, l	er. Pı	includ	tive d	tic co	ple, h	and/o	erred	arteri	eroscl	n, coi	disease, inflammatory	Reyr	disease and Reynaud"s	n, ane	restenosis; venous and	isorde	thrombophlebitis,	lymphangitis, and	a; and	orders	ascula	Ξ	licatic	include trauma such as
lymphangiosarcoma.	red in	e cano	te, bre	atic, e	ch, br	y canc	ions i	lifera	oplast	exam	asia,	prefe	clude	s, athe	ensior	e, infla	itides,	and	nenor	sis; v	atic di	ophle	angitis	edeme	ar disc	eral va	and cancer.	ed inc	traur
ymph	orefer	nclud	rosta	ancre	toma	ırinar	ndica	lysprc	re-ne	s, for	netapl	Jighly	lso in	uch a	ypert	lisease	ascul	lisease	henoi	estenc	ympha	hrom	ympha	ymphe	ascula	eriphe	nd ca	referr	sclude
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			tissue (e.g., vascular injury
~			such as, injury resulting from
•			balloon angioplasty, and
			atheroschlerotic lesions),
•			implant fixation, scarring,
			ischemia reperfusion injury,
			rheumatoid arthritis,
			cerebrovascular disease, renal
 			diseases such as acute renal
			failure, and osteoporosis.
			Additional highly preferred
			indications include stroke,
			graft rejection, diabetic or
			other retinopathies, thrombotic
			and coagulative disorders,
 			vascularitis, lymph
			angiogenesis, sexual disorders,
			age-related macular
			degeneration, and treatment
			/prevention of endometriosis
			and related conditions.
			Additional highly preferred
			indications include fibromas,
			heart disease, cardiac arrest,
			heart valve disease, and
			vascular disease.
			Preferred indications include
 •			blood disorders (e.g., as
		•	described below under
			"Immune Activity", "Blood-
	!		Related Disorders", and/or

					"Cardiovascular Disorders").
	_				Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
					inflammation and
		-			inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
	HDPGT01	587	Regulation of	Assays for the regulation of	A highly preferred
			transcription	transcription through the FAS	indication is diabetes mellitus.
_			through the FAS	promoter element are well-	An additional highly preferred
			promoter element	known in the art and may be	indication is a complication
_			in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
				assess the ability of	diabetic retinopathy, diabetic
				polypeptides of the invention	nephropathy, kidney disease
				(including antibodies and	(e.g., renal failure,
				agonists or antagonists of the	nephropathy and/or other
				invention) to activate the FAS	diseases and disorders as
				promoter element in a reporter	described in the "Renal
				construct and to regulate	Disorders" section below),
				transcription of FAS, a key	diabetic neuropathy, nerve
				enzyme for lipogenesis. FAS	disease and nerve damage

MOLE AND	neomoter is required by many	le a due to dishetic
trans	transcription factors including	neuropathy), blood vessel
SRE	SREBP. Insulin increases FAS	blockage, heart disease, stroke,
gene	gene transcription in livers of	impotence (e.g., due to diabetic
diabe	diabetic mice. This	neuropathy or blood vessel
stim	stimulation of transcription is	blockage), seizures, mental
also	also somewhat glucose	confusion, drowsiness,
edep ebe	dependent. Exemplary assays	nonketotic hyperglycemic-
that	that may be used or routinely	hyperosmolar coma,
modi	modified to test for FAS	cardiovascular disease (e.g.,
prom	promoter element activity (in	heart disease, atherosclerosis,
hepa	hepatocytes) by polypeptides	microvascular disease,
of th	of the invention (including	hypertension, stroke, and other
antib	antibodies and agonists or	diseases and disorders as
antag	antagonists of the invention)	described in the
inclu	include assays disclosed in	"Cardiovascular Disorders"
Xion	Xiong, S., et al., Proc Natl	section below), dyslipidemia,
Acad	Acad Sci U.S.A., 97(8):3948-	endocrine disorders (as
53 (2	53 (2000); Roder, K., et al.,	described in the "Endocrine
Eur	Eur J Biochem, 260(3):743-51	Disorders" section below),
(199	(1999); Oskouian B, et al.,	neuropathy, vision impairment
Bioc	Biochem J, 317 (Pt 1):257-65	(e.g., diabetic retinopathy and
(199)	(1996); Berger, et al., Gene	blindness), ulcers and impaired
199	66:1-10 (1988); and, Cullen,	wound healing, and infection
B., e	B., et al., Methods in Enzymol.	(e.g., infectious diseases and
216:	216:362–368 (1992), the	disorders as described in the
confe	contents of each of which is	"Infectious Diseases" section
herei	herein incorporated by	below, especially of the
refer	reference in its entirety.	urinary tract and skin), carpal
Heps	Hepatocytes that may be used	tunnel syndrome and
acco	according to these assays, such	Dupuytren's contracture).

				as H4IIE cells, are publicly available (e.g., through the	An additional highly preferred indication is obesity and/or
				ATCC) and/or may be	complications associated with
				routinely generated.	obesity. Additional highly
				Exemplary hepatocytes that	preferred indications include
				may be used according to these	weight loss or alternatively,
			_	assays include rat liver	weight gain. Aditional
				hepatoma cell line(s) inducible	highly preferred indications are
				with glucocorticoids, insulin,	complications associated with
				or cAMP derivatives.	insulin resistance.
	HDPHI51	588	Regulation of	Assays for the regulation of	A highly preferred
			transcription	transcription through the FAS	indication is diabetes mellitus.
			through the FAS	promoter element are well-	An additional highly preferred
			promoter element	known in the art and may be	indication is a complication
			in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
				assess the ability of	diabetic retinopathy, diabetic
				polypeptides of the invention	nephropathy, kidney disease
				(including antibodies and	(e.g., renal failure,
				agonists or antagonists of the	nephropathy and/or other
_				invention) to activate the FAS	diseases and disorders as
				promoter element in a reporter	described in the "Renal
_				construct and to regulate	Disorders" section below),
				transcription of FAS, a key	diabetic neuropathy, nerve
				enzyme for lipogenesis. FAS	disease and nerve damage
				promoter is regulated by many	(e.g., due to diabetic
				transcription factors including	neuropathy), blood vessel
				SREBP. Insulin increases FAS	blockage, heart disease, stroke,
				gene transcription in livers of	impotence (e.g., due to diabetic
				diabetic mice. This	neuropathy or blood vessel
				stimulation of transcription is	blockage), seizures, mental
				also somewhat glucose	confusion, drowsiness,

der	dependent. Exemplary assays	nonketotic hyperglycemic-
tha	that may be used or routinely	hyperosmolar coma,
om	modified to test for FAS	cardiovascular disease (e.g.,
pro	promoter element activity (in	heart disease, atherosclerosis,
let let	hepatocytes) by polypeptides	microvascular disease,
) Jo	of the invention (including	hypertension, stroke, and other
ant	antibodies and agonists or	diseases and disorders as
ant	antagonists of the invention)	described in the
inc	include assays disclosed in	"Cardiovascular Disorders"
Xic	Xiong, S., et al., Proc Natl	section below), dyslipidemia,
Ac	Acad Sci U.S.A., 97(8):3948-	endocrine disorders (as
53	53 (2000); Roder, K., et al.,	described in the "Endocrine
Eur	Eur J Biochem, 260(3):743-51	Disorders" section below),
(19	(1999); Oskouian B, et al.,	neuropathy, vision impairment
Bic	Biochem J, 317 (Pt 1):257-65	(e.g., diabetic retinopathy and
(19	(1996); Berger, et al., Gene	blindness), ulcers and impaired
99	66:1-10 (1988); and, Cullen,	wound healing, and infection
B,	B., et al., Methods in Enzymol.	(e.g., infectious diseases and
216	216:362–368 (1992), the	disorders as described in the
cor	contents of each of which is	"Infectious Diseases" section
her	herein incorporated by	below, especially of the
refe	reference in its entirety.	urinary tract and skin), carpal
He	Hepatocytes that may be used	tunnel syndrome and
acc	according to these assays, such	Dupuytren's contracture).
as	as H4IIE cells, are publicly	An additional highly preferred
ava	available (e.g., through the	indication is obesity and/or
AT	ATCC) and/or may be	complications associated with
ron	routinely generated.	obesity. Additional highly
Ex	Exemplary hepatocytes that	preferred indications include
ma	may be used according to these	weight loss or alternatively,
ass	assays include rat liver	weight gain. Aditional

			hepatoma cell line(s) inducible with objectionics insulin	highly preferred indications are
			or cAMP derivatives.	insulin resistance.
HDPHI51	588	Activation of	Assays for the activation of	A highly preferred
		transcription	transcription through the	indication is allergy.
		through STAT6	Signal Transducers and	Another highly preferred
		response element in	Activators of Transcription	indication is asthma.
		immune cells (such	(STAT6) response element are	Additional highly preferred
		as T-cells).	well-known in the art and may	indications include
_			be used or routinely modified	inflammation and
			to assess the ability of	inflammatory disorders.
			polypeptides of the invention	Preferred indications include
			(including antibodies and	blood disorders (e.g., as
			agonists or antagonists of the	described below under
			invention) to regulate STAT6	"Immune Activity", "Blood-
			transcription factors and	Related Disorders", and/or
			modulate the expression of	"Cardiovascular Disorders").
			multiple genes. Exemplary	Preferred indications include
			assays for transcription	autoimmune diseases (e.g.,
			through the STAT6 response	rheumatoid arthritis, systemic
			element that may be used or	lupus erythematosis, multiple
			routinely modified to test	sclerosis and/or as described
			STAT6 response element	below) and
			activity of the polypeptides of	immunodeficiencies (e.g., as
			the invention (including	described below).
			antibodies and agonists or	Preferred indications include
			antagonists of the invention)	neoplastic diseases (e.g.,
			include assays disclosed in	leukemia, lymphoma,
			Berger et al., Gene 66:1-10	melanoma, and/or as described
			(1998); Cullen and Malm,	below under
			Methods in Enzymol 216:362-	"Hyperproliferative

		368 (1992); Henthorn et al.,	Disorders"). Preferred
	•	Proc Natl Acad Sci USA	indications include neoplasms
		85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
_		et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
	-	(1998); Moffatt et al.,	prostate, breast, lung, colon,
		Transplantation 69(7):1521-	pancreatic, esophageal,
		1523 (2000); Curiel et al., Eur	stomach, brain, liver and
		J Immunol 27(8):1982-1987	urinary cancer. Other preferred
		(1997); and Masuda et al., J	indications include benign
		Biol Chem 275(38):29331-	dysproliferative disorders and
		29337 (2000), the contents of	pre-neoplastic conditions, such
		each of which are herein	as, for example, hyperplasia,
		incorporated by reference in its	metaplasia, and/or dysplasia.
		entirety. T cells that may be	Preferred indications include
		used according to these assays	anemia, pancytopenia,
		are publicly available (e.g.,	leukopenia, thrombocytopenia,
		through the ATCC).	Hodgkin's disease, acute
		Exemplary T cells that may be	lymphocytic anemia (ALL),
		used according to these assays	plasmacytomas, multiple
		include the SUPT cell line,	myeloma, Burkitt's lymphoma,
		which is a suspension culture	arthritis, AIDS, granulomatous
		of IL-2 and IL-4 responsive T	disease, inflammatory bowel
-		cells.	disease, sepsis, neutropenia,
-			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted
			organs and tissues,
-			hemophilia, hypercoagulation,
			diabetes mellitus, endocarditis,
			meningitis, and Lyme Disease.
			An additional preferred

				indication is infection (e.g., an infectious disease as described
 				below under "Infectious
				Disease").
HDPJM30	289	Production of	MCP-1 FMAT. Assays for	A highly preferred
		MCP-1	immunomodulatory proteins	embodiment of the invention
			that are produced by a large	includes a method for
		-	variety of cells and act to	stimulating (e.g., increasing)
			induce chemotaxis and	MCP-1 production. An
			activation of monocytes and T	alternative highly preferred
			cells are well known in the art	embodiment of the invention
			and may be used or routinely	includes a method for
			modified to assess the ability	inhibiting (e.g., reducing)
			of polypeptides of the	MCP-1 production. A highly
			invention (including antibodies	S.
			and agonists or antagonists of	infection (e.g., an infectious
			the invention) to mediate	disease as described below
			immunomodulation, induce	under "Infectious Disease").
			chemotaxis, and modulate	Additional highly preferred
			immune cell activation.	indications include
			Exemplary assays that test for	inflammation and
			immunomodulatory proteins	inflammatory disorders.
			evaluate the production of cell	Preferred indications include
			surface markers, such as	blood disorders (e.g., as
		-	monocyte chemoattractant	described below under
			protein (MCP), and the	"Immune Activity", "Blood-
			activation of monocytes and T	Related Disorders", and/or
			cells. Such assays that may be	"Cardiovascular Disorders").
			used or routinely modified to	Highly preferred indications
			test immunomodulatory and	include autoimmune diseases
			diffferentiation activity of	(e.g., rheumatoid arthritis,

systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as		leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL),	plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis. AIDS. granulomatous	disease, inflammatory bowel disease, sepsis, neutropenia,			diabetes mellitus, endocarditis,	meningitis (bacterial and viral), Lyme Disease, asthma, and allergy Preferred	indications also include neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as described below under	"Hyperproliferative	Disorders"). Highly preferred indications include neoplasms
polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in Miraglia et al., J Biomolecular Screening 4:193- 204(1999); Rowland et al.,	"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and	Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); and Verhasselt et al., J Immunol	158:2919-2925 (1997), the contents of each of which are	herein incorporated by reference in its entirety.	Human dendritic cells that may be used according to these	assays may be isolated using techniques disclosed herein or	Otherwise known in the art. Human dendritic cells are antigen presenting cells in	suspension culture, which, when activated by antigen	and/or cytokines, initiate and upregulate T cell proliferation	and functional activities.	
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					and cancers, such as, leukemia.
					lymphoma, prostate, breast,
					lung, colon, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer. Other
					preferred indications include
	•		_		benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	HDPJM30	589	Regulation of	Assays for the regulation of	A highly preferred
			transcription	transcription through the FAS	indication is diabetes mellitus.
			through the FAS	promoter element are well-	An additional highly preferred
			promoter element	known in the art and may be	indication is a complication
			in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
				assess the ability of	diabetic retinopathy, diabetic
				polypeptides of the invention	nephropathy, kidney disease
				(including antibodies and	(e.g., renal failure,
				agonists or antagonists of the	nephropathy and/or other
				invention) to activate the FAS	diseases and disorders as
	•			promoter element in a reporter	described in the "Renal
•				construct and to regulate	Disorders" section below),
				transcription of FAS, a key	diabetic neuropathy, nerve
				enzyme for lipogenesis. FAS	disease and nerve damage
				promoter is regulated by many	(e.g., due to diabetic
				transcription factors including	neuropathy), blood vessel
_	-			SREBP. Insulin increases FAS	blockage, heart disease, stroke,
_	-			gene transcription in livers of	impotence (e.g., due to diabetic
				diabetic mice. This	neuropathy or blood vessel
				stimulation of transcription is	blockage), seizures, mental

	also somewhat glucose	confusion, drowsiness,
	dependent. Exemplary assays	nonketotic hyperglycemic-
	that may be used or routinely	hyperosmolar coma,
	modified to test for FAS	cardiovascular disease (e.g.,
	promoter element activity (in	heart disease, atherosclerosis,
	hepatocytes) by polypeptides	microvascular disease,
	of the invention (including	hypertension, stroke, and other
	antibodies and agonists or	diseases and disorders as
	antagonists of the invention)	described in the
	include assays disclosed in	"Cardiovascular Disorders"
	Xiong, S., et al., Proc Natl	section below), dyslipidemia,
	Acad Sci U.S.A., 97(8):3948-	endocrine disorders (as
	53 (2000); Roder, K., et al.,	described in the "Endocrine
	Eur J Biochem, 260(3):743-51	Disorders" section below),
	(1999); Oskouian B, et al.,	neuropathy, vision impairment
	Biochem J, 317 (Pt 1):257-65	(e.g., diabetic retinopathy and
	(1996); Berger, et al., Gene	blindness), ulcers and impaired
	66:1-10 (1988); and, Cullen,	
	B., et al., Methods in Enzymol.	(e.g., infectious diseases and
	216:362–368 (1992), the	disorders as described in the
	contents of each of which is	"Infectious Diseases" section
	herein incorporated by	below, especially of the
	reference in its entirety.	urinary tract and skin), carpal
	Hepatocytes that may be used	tunnel syndrome and
-	according to these assays, such	Dupuytren's contracture).
	as H4IIE cells, are publicly	An additional highly preferred
	available (e.g., through the	indication is obesity and/or
	ATCC) and/or may be	complications associated with
	routinely generated.	obesity. Additional highly
	Exemplary hepatocytes that	preferred indications include
	may be used according to these	weight loss or alternatively,

			assays include rat liver	weight gain. Aditional
			nepatoma cell line(s) inducible with glucocorticoids, insulin.	highly preferred indications are complications associated with
			or cAMP derivatives.	insulin resistance.
HDPJM30	589	Activation or	This reporter assay measures	
		inhibition of	activation or inhibition of the	
		transcription	NFkB signaling pathway in	
		through NFKB	Ku812 human basophil cell	
		response element in	line. Assays for the activation	
	-	immune cells (such	or inhibition of transcription	
		as basophils).	through the NFKB response	
			element are well-known in the	
			art and may be used or	
			routinely modified to assess	
			the ability of polypeptides of	
			the invention (including	
			antibodies and agonists or	
			antagonists of the invention) to	
			regulate NFKB transcription	
			factors and modulate	
			expression of	
			immunomodulatory genes.	
			NFkB is important in the	
			pathogenesis of asthma.	
			Exemplary assays for	
			transcription through the	
			NFKB response element that	
			may be used or rountinely	
			modified to test NFKB-	
			response element activity of	
			polypeptides of the invention	

(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone	et al, Int Arch Allergy	Immunol 114(3):207-17	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Cells were pretreated with SID	supernatants or controls for 15-	18 hours, and then 10 ng/mL	of TNF was added to stimulate	the NFkB reporter. SEAP	activity was measured after 48	hours. Basophils that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary human basophil	cell lines that may be used	according to these assays	include Ku812, originally	established from a patient with	chronic myelogenous	leukemia. It is an immature
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	Highly preferred indications include diabetes, myopathy, muscle cell atrophy, cancers of muscle (such as, rhabdomyoma, and rhabdosarcoma), cardiovascular disorders (such as congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart valve disease, vascular disease, and also as described below under "Cardiovascular Disorders"), stimulating myoblast proliferation.
prebasophilic cell line that can be induced to differentiate into mature basophils. See, Kishi et al., Leuk Res. 9:381-390 (1985); Blom et al., Eur J Immunol. 22:2025-32 (1992), where the contents of each are herein incorporated by reference in its entirety.	Assays for muscle cell proliferation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit myoblast cell proliferation. Exemplary assays for myoblast cell proliferation that may be used or routinely modified to test activity of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) include, for example, assays disclosed in: Soeta, C., et al. "Possible role for the c-ski gene in the proliferation of
	Myoblast cell proliferation
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	HDPMM88

skeletal muscles of rats" Dev	Growth Differ Apr;43(2):155-	64 (2001); Ewton DZ, et al.,	"IGF binding proteins-4, -5	and -6 may play specialized	roles during L6 myoblast	proliferation and	differentiation" J Endocrinol	Mar;144(3):539-53 (1995);	and, Pampusch MS, et	al.,"Effect of transforming	growth factor beta on	proliferation of L6 and	embryonic porcine myogenic	cells" J Cell Physiol	Jun;143(3):524-8 (1990); the	contents of each of which are	herein incorporated by	reference in their entirety.	Exemplary myoblast cells that	may be used according to these	assays include the rat myoblast	L6 cell line. Rat myoblast L6	cells are an adherent rat	myoblast cell line, isolated	from primary cultures of rat	thigh muscle, that fuse to form	multinucleated myotubes and	striated fibers after culture in	differentiation media.	
																							-							SEAP in HIB/CRE
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This reporter assay measures	activation or inhibition of the	NFkB signaling pathway in	Ku812 human basophil cell	line. Assays for the activation	or inhibition of transcription	through the NFKB response	element are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate NFKB transcription	factors and modulate	expression of	immunomodulatory genes.	NFkB is important in the	pathogenesis of asthma.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene
Activation or	inhibition of	transcription	through NFKB	response element in	immune cells (such	as basophils).																								
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66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone	et al, Int Arch Allergy	Immunol 114(3):207-17	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Cells were pretreated with SID	supernatants or controls for 15-	18 hours, and then 10 ng/mL	of TNF was added to stimulate	the NFkB reporter. SEAP	activity was measured after 48	hours. Basophils that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary human basophil	cell lines that may be used	according to these assays	include Ku812, originally	established from a patient with	chronic myelogenous	leukemia. It is an immature	prebasophilic cell line that can	be induced to differentiate into	mature basophils. See, Kishi et	al., Leuk Res. 9:381-390
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				_																										

				(1985); Blom et al., Eur J	
				Immunol. 22:2025-32 (1992), where the contents of each are	
	_	=		herein incorporated by	
				reference in its entirety.	
	HDPNC61	591	Activation of	Assays for the activation of	A highly preferred indication
			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
			response element	well-known in the art and may	Additional highly preferred
		-	(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
			*	polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
				invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
				functions. For example, a	nephropathy and/or other
				3T3-L1/CRE reporter assay	diseases and disorders as
				may be used to identify factors	described in the "Renal
-				that activate the cAMP	Disorders" section below),
				signaling pathway. CREB	diabetic neuropathy, nerve
				plays a major role in	disease and nerve damage
•				adipogenesis, and is involved	(e.g., due to diabetic
				in differentiation into	neuropathy), blood vessel
				adipocytes. CRE contains the	blockage, heart disease, stroke,
				binding sequence for the	impotence (e.g., due to diabetic
				transcription factor CREB	neuropathy or blood vessel
				(CRE binding protein).	blockage), seizures, mental

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confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	Additional highly preferred	indications are complications	associated with insulin	resistance.		
Exemplary assays for	transcription through the	cAMP response element that	may be used or routinely	modified to test cAMP-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch	et al., Mol Cell Biol	20(3):1008-1020 (2000); and	Klemm et al., J Biol Chem	273:917-923 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. Pre-	adipocytes that may be used	according to these assays are	publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary mouse adipocyte	cells that may be used	according to these assays
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			include 3T3-L1 cells, 3T3-L1	
	_		is an adherent mouse	
	_		preadipocyte cell line that is a	
			continuous substrain of 3T3	
			fibroblast cells developed	
			through clonal isolation and	
_			undergo a pre-adipocyte to	
			adipose-like conversion under	
			appropriate differentiation	
			conditions known in the art.	
HDPNC61	591	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include asthma, allergy,
		through GAS	Gamma Interferon Activation	hypersensitivity reactions,
		response element in	Site (GAS) response element	inflammation, and
	_	immune cells (such	are well-known in the art and	inflammatory disorders.
		as eosinophils).	may be used or routinely	Additional highly preferred
			modified to assess the ability	indications include immune
			of polypeptides of the	and hematopoietic disorders
			invention (including antibodies	(e.g., as described below under
			and agonists or antagonists of	"Immune Activity", and
			the invention) to modulate	"Blood-Related Disorders"),
			gene expression (commonly	autoimmune diseases (e.g.,
			via STAT transcription factors)	rheumatoid arthritis, systemic
			involved in a wide variety of	lupus erythematosis, Crohn"s
			cell functions. Exemplary	disease, multiple sclerosis
			assays for transcription	and/or as described below),
			through the GAS response	immunodeficiencies (e.g., as
			element that may be used or	described below), boosting an
	-		routinely modified to test	eosinophil-mediated immune
			GAS-response element activity	response and, alternatively,
			of polypeptides of the	suppressing an eosinophil-

mediated immune response.		
invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995); the contents of each of which are herein incorporated by reference in its entirety. Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) to activate or inhibit activation of immune cells include assays disclosed and/or cited in: Mayumi M., "EoL-1, a human eosinophilic cell line" Leuk Lymphoma; Jun;7(3):243-50 (1992); Bhattacharya S, "Granulocyte macrophage colony-

stimulating factor and	interleukin-5 activate STAT5	and induce CISI mRNA in	human peripheral blood	eosinophils" Am J Respir Cell	Mol Biol; Mar;24(3):312-6	(2001); and, Du J, et al.,	"Engagement of the CrkL	adapter in interleukin-5	signaling in eosinophils" J Biol	Chem; Oct 20;275(42):33167-	75 (2000); the contents of each	of which are herein	incorporated by reference in its	entirety. Exemplary cells that	may be used according to these	assays include eosinophils.	Eosinophils are a type of	immune cell important in the	late stage of allergic reactions;	they are recruited to tissues	and mediate the inflammtory	response of late stage allergic	reaction. Increases in GAS	mediated transcription in	eosinophils is typically a result	of STAT activation, normally a	direct consequence of	interleukin or other cytokine	receptor stimulation (e.g. IL3,	IL5 or GMCSF).
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HDPNC61	591	Activation of	Kinase assay. Kinase assays,	A highly preferred
		Endothelial Cell	for example an Elk-1 kinase	embodiment of the invention
		ERK Signaling	assay, for ERK signal	includes a method for
		Pathway.	transduction that regulate cell	stimulating endothelial cell
			proliferation or differentiation	growth. An alternative highly
			are well known in the art and	preferred embodiment of the
			may be used or routinely	invention includes a method
			modified to assess the ability	for inhibiting endothelial cell
			of polypeptides of the	growth. A highly preferred
			invention (including antibodies	embodiment of the invention
			and agonists or antagonists of	includes a method for
			the invention) to promote or	stimulating endothelial cell
			inhibit cell proliferation,	proliferation. An alternative
			activation, and differentiation.	highly preferred embodiment
			Exemplary assays for ERK	of the invention includes a
			kinase activity that may be	method for inhibiting
			used or routinely modified to	endothelial cell proliferation.
			test ERK kinase-induced	A highly preferred
			activity of polypeptides of the	embodiment of the invention
			invention (including antibodies	includes a method for
			and agonists or antagonists of	stimulating apoptosis of
			the invention) include the	endothelial cells. An
			assays disclosed in Forrer et	alternative highly preferred
			al., Biol Chem 379(8-9):1101-	embodiment of the invention
			1110 (1998); Berra et al.,	includes a method for
			Biochem Pharmacol	inhibiting (e.g., decreasing)
			60(8):1171-1178 (2000);	apoptosis of endothelial cells.
			Gupta et al., Exp Cell Res	A highly preferred
			247(2):495-504 (1999); Chang	embodiment of the invention
			and Karin, Nature	includes a method for
			410(6824):37-40 (2001); and	stimulating (e.g., increasing)

endothelial cell activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of	(e.g., decreasing) and/or inactivating endothelial cells. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell differentiation. An alternative highly preferred embodiment	of the invention includes a method for inhibiting endothelial cell differentiation. A highly preferred embodiment of the invention includes a method for stimulating angiogenisis. An alternative highly preferred	embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a method for reducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing
Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells	(HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	
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cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as	described below under "Hyperproliferative	Disorders"), and disorders of the cardiovascular system	(e.g., heart disease, congestive heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly
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preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	innibit angiogenesis and/or	caldiovascularizationi. Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and
prefe	stimu	cardi	prete		High	inclu	to tre	lenke	sarco	Highl	inclu	snch	hema	caver	telang	angio	hema	angio	haem	lymbl	lympl	prefer	incluc	prosta	pancr	stoma	urinar	indica	dyspre
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pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	dispasses the ac acute renal
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failure, and osteoporosis.
 Additional highly preferred indications include stroke,
graft rejection, diabetic or
other retinopathies, thrombotic
and coagulative disorders,
vascularitis, lymph
angiogenesis, sexual disorders,
age-related macular
degeneration, and treatment
/prevention of endometriosis
and related conditions.
Additional highly preferred
indications include fibromas,
heart disease, cardiac arrest,
heart valve disease, and
vascular disease.
Preferred indications include
blood disorders (e.g., as
 described below under
"Immune Activity", "Blood-
Related Disorders", and/or
 "Cardiovascular Disorders").
Preferred indications include
autoimmune diseases (e.g.,
rheumatoid arthritis, systemic
lupus erythematosis, multiple
 sclerosis and/or as described
below) and
 immunodeficiencies (e.g., as
described below). Additional

				preferred indications include
_				inflammation and
	_			inflammatory disorders (such
				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
 				and Crohn's disease), and pain
				management.
HDPNC61	591	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include neoplastic diseases
		through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
		response element in	Site (GAS) response element	and/or as described below
		immune cells (such	are well-known in the art and	under "Hyperproliferative
		as T-cells).	may be used or routinely	Disorders"). Highly preferred
			modified to assess the ability	indications include neoplasms
			of polypeptides of the	and cancers, such as, for
			invention (including antibodies	example, leukemia, lymphoma
			and agonists or antagonists of	(e.g., T cell lymphoma,
			the invention) to regulate	Burkitt's lymphoma, non-
			STAT transcription factors and	Hodgkins lymphoma,
			modulate gene expression	Hodgkin"s disease),
			involved in a wide variety of	melanoma, and prostate,
			cell functions. Exemplary	breast, lung, colon, pancreatic,
			assays for transcription	esophageal, stomach, brain,
			through the GAS response	liver and urinary cancer. Other
			element that may be used or	preferred indications include
			routinely modified to test	benign dysproliferative
			GAS-response element activity	disorders and pre-neoplastic
			of polypeptides of the	conditions, such as, for
			invention (including antibodies	example, hyperplasia,
			and agonists or antagonists of	metaplasia, and/or dysplasia.

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Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic	lupus erythematosis, multiple sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis.
the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol 216:362-368 (1992): Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Matikainen et al Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the MOLT4 cell line,	that may be used according to	these assays are publicly	available (e.g., through the	ATCC).											
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					Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and	
<u>工</u>	HDPNC61	591	Production of RANTES in bronchial epithelium cells	RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cell-	astillità alle gy.	

mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as RANTES, and the induction of chemotactic responses in immune cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miragila et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Cocchi et al., Science 270(5243):1811-1815 (1995); and Robinson et al., Clin Exp Immunol 101(3):398-407 (1999), the connents of each of which are herein incorporated by reference in its entirety. Epithelial cells were isolated from bronchia/trachea immediately postmorten from																																
	modioted imminity	Evenulary account that test for	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as RANTES,	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Epithelial cells were isolated	from bronchia/trachea	immediately postmortem from	humans who were free of
			_																				-									

			known respiratory diseases. See Wu et al., Am Rev Respir Dis. 132(2):311-20 (1985), the contents of which are herein incorporated by reference in its entirety.	
HDPOJ08	592	Inhibition of squalene synthetase gene transcription.	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	
HDPOJ08	592	Regulation of apoptosis in pancreatic beta cells.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication

	access the ability of	seconstant with diahatar (a a
	nolynentides of the invention	dishetic retinonothy dishetic
	fortypepudes of the lifetiuon	diabetic retinopathy, diabetic
	(including antibodies and	nephropathy, kidney disease
	agonists or antagonists of the	(e.g., renal failure,
	invention) to promote caspase	nephropathy and/or other
	protease-mediated apoptosis.	diseases and disorders as
	Apoptosis in pancreatic beta is	described in the "Renal
	associated with induction and	Disorders" section below),
	progression of diabetes.	diabetic neuropathy, nerve
	Exemplary assays for caspase	disease and nerve damage
	apoptosis that may be used or	(e.g., due to diabetic
	routinely modified to test	neuropathy), blood vessel
	capase apoptosis activity of	blockage, heart disease, stroke,
	polypeptides of the invention	impotence (e.g., due to diabetic
	(including antibodies and	neuropathy or blood vessel
	agonists or antagonists of the	blockage), seizures, mental
-	invention) include the assays	confusion, drowsiness,
	disclosed in: Loweth, AC, et	nonketotic hyperglycemic-
	al., FEBS Lett, 400(3):285-8	hyperosmolar coma,
	(1997); Saini, KS, et al.,	cardiovascular disease (e.g.,
	Biochem Mol Biol Int,	heart disease, atherosclerosis,
	39(6):1229-36 (1996);	microvascular disease,
	Krautheim, A., et al., Br J	hypertension, stroke, and other
	Pharmacol, 129(4):687-94	diseases and disorders as
	(2000); Chandra J, et al.,	described in the
	Diabetes, 50 Suppl 1:S44-7	"Cardiovascular Disorders"
	(2001); Suk K, et al., J	section below), dyslipidemia,
	Immunol, 166(7):4481-9	endocrine disorders (as
_	(2001); Tejedo J, et al., FEBS	described in the "Endocrine
	Lett, 459(2):238-43 (1999);	Disorders" section below),
	Zhang, S., et al., FEBS Lett,	neuropathy, vision impairment

		455(3):315-20 (1999); Lee et	(e.g., diabetic retinopathy and
		al., FEBS Lett 485(2-3): 122-	blindness), ulcers and impaired
		126 (2000); Nor et al., J Vasc	wound healing, and infection
		Res 37(3): 209-218 (2000);	(e.g., infectious diseases and
		and Karsan and Harlan, J	disorders as described in the
		Atheroscler Thromb 3(2): 75-	"Infectious Diseases" section
		80 (1996); the contents of each	below, especially of the
-		of which are herein	urinary tract and skin), carpal
	-	incorporated by reference in its	tunnel syndrome and
		entirety. Pancreatic cells that	Dupuytren's contracture).
		may be used according to these	An additional highly preferred
		assays are publicly available	indication is obesity and/or
		(e.g., through the ATCC)	complications associated with
		and/or may be routinely	obesity. Additional highly
		generated. Exemplary	preferred indications include
		pancreatic cells that may be	weight loss or alternatively,
		used according to these assays	weight gain. Aditional
		include RIN-m. RIN-m is a	highly preferred indications are
-		rat adherent pancreatic beta	complications associated with
		cell insulinoma cell line	insulin resistance.
		derived from a radiation	
		induced transplantable rat islet	
		cell tumor. The cells produce	
		and secrete islet polypeptide	
		hormones, and produce insulin,	
		somatostatin, and possibly	
		glucagon. ATTC: #CRL-2057	
		Chick et al. Proc. Natl. Acad.	
		Sci. 1977 74:628; AF et al.	
		Proc. Natl. Acad. Sci. 1980	
		77:3519.	

HDPOZ56	593	Activation of	Assays for the activation of	Preferred embodiments of the
		transcription	transcription through the	invention include using
		through GAS	Gamma Interferon Activation	polypeptides of the invention
		response element in	Site (GAS) response element	(or antibodies, agonists, or
		epithelial cells	are well-known in the art and	antagonists thereof) in
		(such as HELA	may be used or routinely	detection, diagnosis,
		cells).	modified to assess the ability	prevention, and/or treatment of
			of polypeptides of the	Cancer, Wound Healing, and
			invention (including antibodies	Inflamation. Highly preferred
			and agonists or antagonists of	indications include neoplastic
			the invention) to regulate	diseases (e.g., as described
-			STAT transcription factors and	below under
			modulate gene expression	"Hyperproliferative
			involved in a wide variety of	Disorders"). Highly preferred
			cell functions. Exemplary	indications include neoplasms
			assays for transcription	and cancers, such as, for
			through the GAS response	example, melanoma, and
			element that may be used or	prostate, breast, lung, colon,
			routinely modified to test	pancreatic, esophageal,
			GAS-response element activity	stomach, brain, liver and
			of polypeptides of the	urinary cancer. Other preferred
			invention (including antibodies	indications include benign
			and agonists or antagonists of	dysproliferative disorders and
			the invention) include assays	pre-neoplastic conditions, such
			disclosed in: You M, et al, J	as, for example, hyperplasia,
			Biol Chem, 272(37):23376-	metaplasia, and/or dysplasia.
			23381(1997); Min W, et al.,	Preferred indications include
			Circ Res, 83(8):815-823	include inflammation and
			(1998); Berger et al., Gene	inflammatory disorders.
			66:1-10 (1998); Cullen and	
			Malm, Methods in Enzymol	

	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative
216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Epithelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary epithelial cells that may be used according to these assays include the HELA cell line.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and
	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
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	HDP0Z56

		anontosis Exemnlary assays	highly preferred embodiment
		for INIV and n20 Lines	of the incention includes
		IOI JINN AIIU DOO NIIIASE	or the myennon includes a
		activity that may be used or	method for inhibiting
		routinely modified to test JNK	endothelial cell proliferation.
		and p38 kinase-induced	A highly preferred
		activity of polypeptides of the	embodiment of the invention
		invention (including antibodies	includes a method for
		and agonists or antagonists of	stimulating apoptosis of
		the invention) include the	endothelial cells. An
		assays disclosed in Forrer et	alternative highly preferred
		al., Biol Chem 379(8-9):1101-	embodiment of the invention
		1110 (1998); Gupta et al., Exp	includes a method for
		Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
		(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
		Soc Symp 64:29-48 (1999);	A highly preferred
		Chang and Karin, Nature	embodiment of the invention
		410(6824):37-40 (2001); and	includes a method for
-		Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
		Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
		the contents of each of which	alternative highly preferred
		are herein incorporated by	embodiment of the invention
		reference in its entirety.	includes a method for
-		Endothelial cells that may be	inhibiting (e.g., decreasing) the
		used according to these assays	activation of and/or
		are publicly available (e.g.,	inactivating endothelial cells.
		through the ATCC).	A highly preferred
		Exemplary endothelial cells	embodiment of the invention
		that may be used according to	includes a method for
		these assays include human	stimulating angiogenisis. An
		umbilical vein endothelial cells	alternative highly preferred
		(HUVEC), which are	embodiment of the invention

		endothelial cells which line	includes a method for
		venous blood vessels, and are	inhihiting angiogenesis
-		involved in finations that	hight.
		involved in tunctions that	inginy preferred embodiment
		include, but are not limited to,	of the invention includes a
		angiogenesis, vascular	method for reducing cardiac
		permeability, vascular tone,	hypertrophy. An alternative
		and immune cell extravasation.	highly preferred embodiment
			of the invention includes a
			method for inducing cardiac
			hypertrophy. Highly
	-		preferred indications include
			neoplastic diseases (e.g., as
			described below under
			"Hyperproliferative
			Disorders"), and disorders of
			the cardiovascular system
			(e.g., heart disease, congestive
			heart failure, hypertension,
			aortic stenosis,
			cardiomyopathy, valvular
			regurgitation, left ventricular
			dysfunction, atherosclerosis
			and atherosclerotic vascular
			disease, diabetic nephropathy,
			intracardiac shunt, cardiac
			hypertrophy, myocardial
			infarction, chronic
			hemodynamic overload, and/or
			as described below under
			"Cardiovascular Disorders").
			Highly preferred indications

	include cardiovascular,
	endothelial and/or angiogenic
	disorders (e.g., systemic
	disorders that affect vessels
	such as diabetes mellitus, as
	well as diseases of the vessels
	themselves, such as of the
	arteries, capillaries, veins
	and/or lymphatics). Highly
	preferred are indications that
	stimulate angiogenesis and/or
	cardiovascularization. Highly
	preferred are indications that
	inhibit angiogenesis and/or
	cardiovascularization.
	Highly preferred indications
	include antiangiogenic activity
	to treat solid tumors,
	leukemias, and Kaposi"s
	sarcoma, and retinal disorders.
	Highly preferred indications
	include neoplasms and cancer,
	such as, Kaposi"s sarcoma,
	hemangioma (capillary and
	cavernous), glomus tumors,
	telangiectasia, bacillary
	angiomatosis,
	hemangioendothelioma,
	angiosarcoma,
	haemangiopericytoma,
	lymphangioma,

lymphangiosarcoma. Highly preferred indications also	preferred indications also include cancers such as.	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud's	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured
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														-															

			tissue (e o vascular iniury
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			such as, injury resulting from
			balloon angioplasty, and
			atheroschlerotic lesions),
-			implant fixation, scarring,
-			ischemia reperfusion injury,
			rheumatoid arthritis,
			cerebrovascular disease, renal
			diseases such as acute renal
			failure, and osteoporosis.
			Additional highly preferred
			indications include stroke,
			graft rejection, diabetic or
			other retinopathies, thrombotic
-			and coagulative disorders,
			vascularitis, lymph
-			angiogenesis, sexual disorders,
			age-related macular
•			degeneration, and treatment
-			/prevention of endometriosis
	-		and related conditions.
			Additional highly preferred
			indications include fibromas,
			heart disease, cardiac arrest,
			heart valve disease, and
	-	-	vascular disease.
			Preferred indications include
			blood disorders (e.g., as
			described below under
-			"Immune Activity", "Blood-
			Related Disorders", and/or

upregulated by glucose and	(e.g., due to diabetic
also by certain	neuropathy), blood vessel
proteins/peptides, and	blockage, heart disease, stroke,
disregulation is a key	impotence (e.g., due to diabetic
component in diabetes.	neuropathy or blood vessel
Exemplary assays that may be	blockage), seizures, mental
 used or routinely modified to	confusion, drowsiness,
test for stimulation of insulin	nonketotic hyperglycemic-
secretion (from pancreatic	hyperosmolar coma,
cells) by polypeptides of the	cardiovascular disease (e.g.,
invention (including antibodies	heart disease, atherosclerosis,
and agonists or antagonists of	microvascular disease,
the invention) include assays	hypertension, stroke, and other
disclosed in: Ahren, B., et al.,	diseases and disorders as
Am J Physiol, 277(4 Pt	described in the
2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
al., Endocrinology,	section below), dyslipidemia,
138(9):3735-40 (1997); Kim,	endocrine disorders (as
K.H., et al., FEBS Lett,	described in the "Endocrine
377(2):237-9 (1995); and,	Disorders" section below),
Miraglia S et. al., Journal of	neuropathy, vision impairment
Biomolecular Screening,	(e.g., diabetic retinopathy and
4:193-204 (1999), the contents	blindness), ulcers and impaired
of each of which is herein	wound healing, and infection
incorporated by reference in its	(e.g., infectious diseases and
entirety. Pancreatic cells that	disorders as described in the
may be used according to these	"Infectious Diseases" section
 assays are publicly available	below, especially of the
(e.g., through the ATCC)	urinary tract and skin), carpal
and/or may be routinely	tunnel syndrome and
generated. Exemplary	Dupuytren's contracture).

			pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
HDPSB18	295	Stimulation of insulin secretion from pancreatic beta cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke,

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	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	
	disregulation is a key	component in diabetes.	Exemplary assays that may be	used or routinely modified to	test for stimulation of insulin	secretion (from pancreatic	cells) by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Ahren, B., et al.,	Am J Physiol, 277(4 Pt	2):R959-66 (1999); Li, M., et	al., Endocrinology,	138(9):3735-40 (1997); Kim,	K.H., et al., FEBS Lett,	377(2):237-9 (1995); and,	Miraglia S et. al., Journal of	Biomolecular Screening,	4:193-204 (1999), the contents	of each of which is herein	incorporated by reference in its	entirety. Pancreatic cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC)	and/or may be routinely	generated. Exemplary	pancreatic cells that may be	used according to these assays	
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			cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
HDPSH53	965	Stimulation of Calcium Flux in pancreatic beta cells.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic
			responsive signaling pathways and alterations in cell	neuropathy or blood vessel blockage), seizures, mental

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confusion, drowsiness, nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,		microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively.
functions. Exemplary assays that may be used or routinely	modified to measure calcium	flux by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Satin LS, et al.,	Endocrinology, 136(10):4589-	601 (1995);Mogami H, et al.,	Endocrinology, 136(7):2960-6	(1995); Richardson SB, et al.,	Biochem J, 288 (Pt 3):847-51	(1992); and, Meats, JE, et al.,	Cell Calcium 1989 Nov-	Dec;10(8):535-41 (1989), the	contents of each of which is	herein incorporated by	reference in its entirety.	Pancreatic cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary pancreatic cells that	may be used according to these	assays include HITT15 Cells.	HITT15 are an adherent	epithelial cell line established	from Syrian hamster islet cells	transformed with SV40. These
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				cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
HDPSH53	23	969	Production of RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))	RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cellmediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of	

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cytokines, such as RANTES,	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	'Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells
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			(HUVEC), which are	
			endothelial cells which line	
			venous blood vessels, and are	
			involved in functions that	
			include, but are not limited to,	
			angiogenesis, vascular	
			permeability, vascular tone,	
			and immune cell extravasation.	
HDPSP01	597	Production of	MCP-1 FMAT. Assays for	A highly preferred
		MCP-1	immunomodulatory proteins	embodiment of the invention
			that are produced by a large	includes a method for
			variety of cells and act to	stimulating (e.g., increasing)
			induce chemotaxis and	MCP-1 production. An
			activation of monocytes and T	alternative highly preferred
			cells are well known in the art	embodiment of the invention
			and may be used or routinely	includes a method for
			modified to assess the ability	inhibiting (e.g., reducing)
		·	of polypeptides of the	MCP-1 production. A highly
			invention (including antibodies	preferred indication is
			and agonists or antagonists of	infection (e.g., an infectious
			the invention) to mediate	disease as described below
			immunomodulation, induce	under "Infectious Disease").
			chemotaxis, and modulate	Additional highly preferred
			immune cell activation.	indications include
			Exemplary assays that test for	inflammation and
			immunomodulatory proteins	inflammatory disorders.
			evaluate the production of cell	Preferred indications include
			surface markers, such as	blood disorders (e.g., as
			monocyte chemoattractant	described below under
			protein (MCP), and the	"Immune Activity", "Blood-
			activation of monocytes and T	Related Disorders", and/or

	cells. Such assays that may be	"Cardiovascular Disorders")
	used or routinely modified to	Highly preferred indications
	test immunomodulatory and	include autoimmune diseases
	diffferentiation activity of	(e.g., rheumatoid arthritis,
	polypeptides of the invention	systemic lupus erythematosis,
	(including antibodies and	multiple sclerosis and/or as
	agonists or antagonists of the	described below) and
	invention) include assays	immunodeficiencies (e.g., as
	disclosed in Miraglia et al., J	described below). Preferred
-	Biomolecular Screening 4:193-	- j
	204(1999); Rowland et al.,	anemia, pancytopenia,
	"Lymphocytes: a practical	leukopenia, thrombocytopenia,
	approach" Chapter 6:138-160	Hodgkin's disease, acute
	(2000); Satthaporn and	lymphocytic anemia (ALL),
	Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
	45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
	Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
	158:2919-2925 (1997), the	disease, inflammatory bowel
	contents of each of which are	disease, sepsis, neutropenia,
	herein incorporated by	neutrophilia, psoriasis,
	reference in its entirety.	suppression of immune
	Human dendritic cells that may	reactions to transplanted
	be used according to these	organs and tissues,
	assays may be isolated using	hemophilia, hypercoagulation,
	techniques disclosed herein or	diabetes mellitus, endocarditis,
	otherwise known in the art.	meningitis (bacterial and
	Human dendritic cells are	viral), Lyme Disease, asthma,
	antigen presenting cells in	and allergy Preferred
	suspension culture, which,	indications also include
	when activated by antigen	neoplastic diseases (e.g.,
	and/or cytokines, initiate and	leukemia, lymphoma, and/or as

			upregulate T cell proliferation and functional activities.	described below under "Hyperproliferative Disorders" Highly professional
				indications include neoplasms
				and cancers, such as, leukemia,
				lymphoma, prostate, breast,
				lung, colon, pancreatic,
			, and the second	esophageal, stomach, brain,
				liver, and urinary cancer. Other
				preferred indications include
				benign dysproliferative
				disorders and pre-neoplastic
				conditions, such as, for
				example, hyperplasia,
				metaplasia, and/or dysplasia.
HDPSP01	597	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
			of insulin are well-known in	is diabetes mellitus. An
			the art and may be used or	additional highly preferred
			routinely modified to assess	indication is a complication
			the ability of polypeptides of	associated with diabetes (e.g.,
			the invention (including	diabetic retinopathy, diabetic
			antibodies and agonists or	nephropathy, kidney disease
			antagonists of the invention) to	(e.g., renal failure,
			stimulate insulin secretion.	nephropathy and/or other
			For example, insulin secretion	diseases and disorders as
			is measured by FMAT using	described in the "Renal
			anti-rat insulin antibodies.	Disorders" section below),
			Insulin secretion from	diabetic neuropathy, nerve
			pancreatic beta cells is	disease and nerve damage
			upregulated by glucose and	(e.g., due to diabetic
			also by certain	neuropathy), blood vessel

	proteins/peptides, and	blockage, heart disease, stroke,
	disregulation is a key	impotence (e.g., due to diabetic
	component in diabetes.	neuropathy or blood vessel
	Exemplary assays that may be	blockage), seizures, mental
	used or routinely modified to	confusion, drowsiness,
	test for stimulation of insulin	nonketotic hyperglycemic-
	secretion (from pancreatic	hyperosmolar coma,
	cells) by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
-	the invention) include assays	hypertension, stroke, and other
	disclosed in: Shimizu, H., et	diseases and disorders as
	al., Endocr J, 47(3):261-9	described in the
	(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
	Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
	17 (1999); Filipsson, K., et al.,	endocrine disorders (as
	Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
	(1998); Olson, L.K., et al., J	Disorders" section below),
	Biol Chem, 271(28):16544-52	neuropathy, vision impairment
	(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
	Journal of Biomolecular	blindness), ulcers and impaired
	Screening, 4:193-204 (1999),	wound healing, and infection
	the contents of each of which	(e.g., infectious diseases and
	is herein incorporated by	disorders as described in the
	reference in its entirety.	"Infectious Diseases" section
	Pancreatic cells that may be	below, especially of the
	used according to these assays	urinary tract and skin), carpal
	are publicly available (e.g.,	tunnel syndrome and
	through the ATCC) and/or	Dupuytren's contracture).
	may be routinely generated.	An additional highly preferred
	Exemplary pancreatic cells that	indication is obesity and/or

				may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78:	complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
日	HDPSP54	298	Activation of Endothelial Cell JNK Signaling Pathway.	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation,	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell

proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting	endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for	stimulating apoptosis of endothelial cells. An alternative highly preferred	embodiment of the invention includes a method for inhibiting apoptosis of endothelial cells.	highly preferred embodiment of the invention includes a method for stimulating	endothelial cell activation. An alternative highly preferred embodiment of the invention includes a method for	inhibiting the activation of and/or inactivating endothelial cells. A highly preferred	embodiment of the invention includes a method for stimulating angiogenisis. An alternative highly preferred	embodiment of the invention includes a method for
activation, and apoptosis. Exemplary assays for JNK kinase activity that may be used or routinely modified to	test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of	the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Svmp 64:29-48 (1999):	Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol	biol /1(3-4):4/9-500 (1999); the contents of each of which are herein incorporated by reference in its entirety	Endothelial cells that may be used according to these assays are publicly available (e.g.,	through the ATCC). Exemplary endothelial cells that may be used according to these assays include human	umbilical vein endothelial cells (HUVEC), which are

angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as	"Hyperproliferative Disorders"), and disorders of the cardiovascular system	(e.g., heart disease, congestive heart failure, hypertension, aortic stenosis,	regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular	disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic	hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular

preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury
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such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").
such as,	palloon	atherosc	implant	ischemia	rheumat	cerebrov	diseases	failure, a	Addition	indicatio	graft reje	other ret	and coag	vascular	angioger	age-relat	degenera	/preventi	and relat	Addition	indicatio	heart dis	heart val	vascular	Preferred	blood dis	described	, Immune	Related I	"Cardiov
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					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
					inflammation and
					inflammatory disorders (such
_					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
	HDPSP54	869	Regulation of	Caspase Apoptosis. Assays	A highly preferred
			apoptosis in	for caspase apoptosis are well	indication is diabetes mellitus.
			pancreatic beta	known in the art and may be	An additional highly preferred
			cells.	used or routinely modified to	indication is a complication
				assess the ability of	associated with diabetes (e.g.,
				polypeptides of the invention	diabetic retinopathy, diabetic
				(including antibodies and	nephropathy, kidney disease
				agonists or antagonists of the	(e.g., renal failure,
				invention) to promote caspase	nephropathy and/or other
				protease-mediated apoptosis.	diseases and disorders as
				Apoptosis in pancreatic beta is	described in the "Renal
				associated with induction and	Disorders" section below),
				progression of diabetes.	diabetic neuropathy, nerve
				Exemplary assays for caspase	disease and nerve damage
			-	apoptosis that may be used or	(e.g., due to diabetic

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		capase apoptosis activity of	blockage, heart disease, stroke,
		polypeptides of the invention	impotence (e.g., due to diabetic
		(including antibodies and	neuropathy or blood vessel
		agonists or antagonists of the	blockage), seizures, mental
		invention) include the assays	confusion, drowsiness,
		disclosed in: Loweth, AC, et	nonketotic hyperglycemic-
		al., FEBS Lett, 400(3):285-8	hyperosmolar coma,
_		(1997); Saini, KS, et al.,	cardiovascular disease (e.g.,
		Biochem Mol Biol Int,	heart disease, atherosclerosis,
		39(6):1229-36 (1996);	microvascular disease,
		Krautheim, A., et al., Br J	hypertension, stroke, and other
		Pharmacol, 129(4):687-94	diseases and disorders as
		(2000); Chandra J, et al.,	described in the
		Diabetes, 50 Suppl 1:S44-7	"Cardiovascular Disorders"
		(2001); Suk K, et al., J	section below), dyslipidemia,
		Immunol, 166(7):4481-9	endocrine disorders (as
		(2001); Tejedo J, et al., FEBS	described in the "Endocrine
		Lett, 459(2):238-43 (1999);	Disorders" section below),
		Zhang, S., et al., FEBS Lett,	neuropathy, vision impairment
		455(3):315-20 (1999); Lee et	(e.g., diabetic retinopathy and
	-	al., FEBS Lett 485(2-3): 122-	blindness), ulcers and impaired
		126 (2000); Nor et al., J Vasc	wound healing, and infection
		Res 37(3): 209-218 (2000);	(e.g., infectious diseases and
•		and Karsan and Harlan, J	disorders as described in the
		Atheroscler Thromb 3(2): 75-	"Infectious Diseases" section
		80 (1996); the contents of each	below, especially of the
 		of which are herein	urinary tract and skin), carpal
		incorporated by reference in its	tunnel syndrome and
		entirety. Pancreatic cells that	Dupuytren's contracture).
		may be used according to these	An additional highly preferred

			assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include RIN-m. RIN-m is a rat adherent pancreatic beta cell insulinoma cell line derived from a radiation induced transplantable rat islet	indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
			cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1977 74:628; AF et al. Proc. Natl. Acad. Sci. 1980 77:3519.	
HDPSP54	865	Production of IL-10 and activation of T-cells.	Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of	Highly preferred indications include allergy and asthma. Additional highly preferred indications include immune and hematopoietic disorders
			polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells.	(e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s

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	sclerosia	ed below	ies (e.g.	boostin	nune	pressing	nune																							
	nultiple	describ	eficienc	below)	ated im	and sup	ated im																							
	disease, multiple sclerosis	and/or as described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response.	ı																					
	4)											7	se	896	I.			ıtics;		are				says		ay be	h2	are	te	フュ
	that ma	nodified	J(ıntibodia	uding	nists of	ulate IL-	T-cell	de, for	ich as	ited in:	ıl., "Th-	ic disea	4): 956-9	et al., "	directed	=	Therapeu); the	f which	d by	ntirety.	lat may l	these ass	IL10	cells ma	ker of T	h2 cells	nat secre	TIA II 10 II 12 II 5 and II 6
	assays	atinely r	ability o	es and a	on (incl	antago.	to mode	and/or	on inclu	issays su	und/or ci	DS, et a	n allerg	ıll; 56 (²	d Cohn,	2 cell-6	asthma	ogy & 1	6 (2000	each of	rporate	n their e	cells th	ding to 1	2 cells.	om Th2	is a mar	ion. T	cells th	II 12 II
	Exemplary assays that may be	used or routinely modified to	assess the ability of	polypeptides and antibodies of	the invention (including	agonists or antagonists of the	invention) to modulate IL-10	production and/or T-cell	proliferation include, for	example, assays such as	disclosed and/or cited in:	Robinson, DS, et al., "Th-2	cytokines in allergic disease"	Br Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the	contents of each of which are	herein incorporated by	reference in their entirety.	Exemplary cells that may be	used according to these assays	include Th2 cells. IL10	secreted from Th2 cells may be	measured as a marker of Th2	cell activation. Th2 cells are	a class of T cells that secrete	1 II 10
	Ë	sn	ass	bo	the	age	in	pre	pre	ex	dis	Ro	<u>5</u>	Br	(5	he	the	Ph	88	[O	he	ref	Ex	nse	inc	sec	me	cel	ac	ì
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				differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated	
EH .	HDPUW68	009	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly
				invention (including antibodies and agonists or antagonists of	invention includes a method for stimulating (e.g.,

			the throughout (motivation)	in organization of property
			the invention) include tite	mereasing) ampocyte
			assays disclosed in Forrer et	activation. An alternative
			al., Biol Chem 379(8-9):1101-	highly preferred embodiment
			1110 (1998); Le Marchand-	of the invention includes a
			Brustel Y, Exp Clin	method for inhibiting the
			Endocrinol Diabetes	activation of (e.g., decreasing)
			107(2):126-132 (1999);	and/or inactivating adipocytes.
-			Kyriakis JM, Biochem Soc	Highly preferred indications
			Symp 64:29-48 (1999); Chang	include endocrine disorders
			and Karin, Nature	(e.g., as described below under
			410(6824):37-40 (2001); and	"Endocrine Disorders").
			Cobb MH, Prog Biophys Mol	Highly preferred indications
			Biol 71(3-4):479-500 (1999);	also include neoplastic
			the contents of each of which	diseases (e.g., lipomas,
			are herein incorporated by	liposarcomas, and/or as
			reference in its entirety.	described below under
_			Mouse adipocyte cells that	"Hyperproliferative
	-		may be used according to these	Disorders"). Preferred
			assays are publicly available	indications include blood
			(e.g., through the ATCC).	disorders (e.g., hypertension,
			Exemplary mouse adipocyte	congestive heart failure, blood
			cells that may be used	vessel blockage, heart disease,
			according to these assays	stroke, impotence and/or as
			include 3T3-L1 cells. 3T3-L1	described below under
			is an adherent mouse	"Immune Activity",
		-	preadipocyte cell line that is a	"Cardiovascular Disorders",
	-		continuous substrain of 3T3	and/or "Blood-Related
			fibroblast cells developed	Disorders"), immune disorders
			through clonal isolation and	(e.g., as described below under
			undergo a pre-adipocyte to	"Immune Activity"), neural
			adipose-like conversion under	disorders (e.g., as described

below under "Neural Activity and Neurological Diseases"), and infection (e.g., as described below under "Infectious Disease").	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic	(e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic	neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease,
appropriate differentiation conditions known in the art.			
	<u>.</u>		
			·

		hypertension, stroke, and other	nd other
		diseases and disorders as	as
		described in the	
		"Cardiovascular Disorders"	lers"
		section below), dyslipidemia,	demia,
-		endocrine disorders (as	
		described in the "Endocrine	crine
		Disorders" section below),	w),
		neuropathy, vision impairment	airment
	-	(e.g., diabetic retinopathy and	hy and
	-	blindness), ulcers and impaired	mpaired
		wound healing, infection (e.g.,	on (e.g.,
		infectious diseases and	
		disorders as described in the	n the
		"Infectious Diseases" section	ection
		below (particularly of the	he
		urinary tract and skin).	An
		additional highly preferred	red
		indication is obesity and/or	d/or
		complications associated with	d with
		obesity. Additional highly	hly
	***	preferred indications include	clude
		weight loss or alternatively,	vely,
		weight gain. Add	Additional
		highly preferred indications are	ions are
		complications associated with	d with
		insulin resistance.	
		Additional highly preferred	rred
	·	indications are disorders of the	s of the
		musculoskeletal systems	S
		including myopathies,	

				muscular dystrophy, and/or as
				described herein.
				Additional highly preferred
				indications include,
				hypertension, coronary artery
				disease, dyslipidemia,
				gallstones, osteoarthritis,
				degenerative arthritis, eating
				disorders, fibrosis, cachexia,
				and kidney diseases or
				disorders. Preferred
	2000			indications include neoplasms
				and cancer, such as,
				lymphoma, leukemia and
				breast, colon, and kidney
				cancer. Additional preferred
			-	indications include melanoma,
				prostate, lung, pancreatic,
	-			esophageal, stomach, brain,
		a-		liver, and urinary cancer.
				Highly preferred indications
				include lipomas and
				liposarcomas. Other preferred
				indications include benign
				dysproliferative disorders and
				pre-neoplastic conditions, such
				as, for example, hyperplasia,
				metaplasia, and/or dysplasia.
HDPUW68	009	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,

		1 1 1 1 1 1 1 1
 response element in	(SKE) are well-known in the	reducing) Tink alpha
immune cells (such	art and may be used or	production. An alternative
as T-cells).	routinely modified to assess	preferred embodiment of the
`	the ability of polypeptides of	invention includes a method
	the invention (including	for stimulating (e.g.,
	antibodies and agonists or	increasing) TNF alpha
	antagonists of the invention) to	production. Preferred
	regulate the serum response	indications include blood
	factors and modulate the	disorders (e.g., as described
	expression of genes involved	below under "Immune
	in growth. Exemplary assays	Activity", "Blood-Related
	for transcription through the	Disorders", and/or
	SRE that may be used or	"Cardiovascular Disorders"),
	routinely modified to test SRE	Highly preferred indications
	activity of the polypeptides of	include autoimmune diseases
	the invention (including	(e.g., rheumatoid arthritis,
	antibodies and agonists or	systemic lupus erythematosis,
	antagonists of the invention)	Crohn's disease, multiple
	include assays disclosed in	sclerosis and/or as described
	Berger et al., Gene 66:1-10	below), immunodeficiencies
 	(1998); Cullen and Malm,	(e.g., as described below),
	Methods in Enzymol 216:362-	boosting a T cell-mediated
	368 (1992); Henthorn et al.,	immune response, and
	Proc Natl Acad Sci USA	suppressing a T cell-mediated
	85:6342-6346 (1988); and	immune response. Additional
	Black et al., Virus Genes	highly preferred indications
	12(2):105-117 (1997), the	include inflammation and
	content of each of which are	inflammatory disorders, and
	herein incorporated by	treating joint damage in
	reference in its entirety. T	patients with rheumatoid
	cells that may be used	arthritis. An additional highly

preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally,	highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal stomach brain	esopnageal, stomach, orani, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, thodokin's disease acute	lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous
according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2	dependent suspension culture of T cells with cytotoxic activity.		

				disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
HDPUW68	009	Stimulation of Calcium Flux in pancreatic beta cells.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic

	an influx of calcium, leading to	blockage, heart disease, stroke,
	activation of calcium	impotence (e.g., due to diabetic
	responsive signaling pathways	neuropathy or blood vessel
	and alterations in cell	blockage), seizures, mental
	functions. Exemplary assays	confusion, drowsiness,
	that may be used or routinely	nonketotic hyperglycemic-
-	modified to measure calcium	hyperosmolar coma,
	flux by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Satin LS, et al.,	diseases and disorders as
	Endocrinology, 136(10):4589-	described in the
	601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
	Endocrinology, 136(7):2960-6	section below), dyslipidemia,
	(1995); Richardson SB, et al.,	endocrine disorders (as
	Biochem J, 288 (Pt 3):847-51	described in the "Endocrine
	(1992); and, Meats, JE, et al.,	Disorders" section below),
	Cell Calcium 1989 Nov-	neuropathy, vision impairment
	Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
	contents of each of which is	blindness), ulcers and impaired
	herein incorporated by	wound healing, and infection
	reference in its entirety.	(e.g., infectious diseases and
	Pancreatic cells that may be	disorders as described in the
	used according to these assays	"Infectious Diseases" section
	are publicly available (e.g.,	below, especially of the
	through the ATCC) and/or	urinary tract and skin), carpal
	may be routinely generated.	tunnel syndrome and
	Exemplary pancreatic cells that	Dupuytren's contracture).
	may be used according to these	An additional highly preferred
	assays include HITT15 Cells.	indication is obesity and/or

			HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78:	complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
HDPUW68	009	Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway	Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for Pl3 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival.	A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred embodiment of the invention includes a method for stimulating muscle cell proliferation. In a specific embodiment, skeletal muscle

cell proliferation is stimulated. An alternative highly preferred embodiment of the invention includes a method for inhibiting muscle cell	proliferation. In a specific embodiment, skeletal muscle cell proliferation is inhibited. A preferred embodiment of the invention includes a	method for stimulating muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is	stimulated. An alternative highly preferred embodiment of the invention includes a method for inhibiting muscle cell differentiation. In a	specific embodiment, skeletal muscle cell differentiation is inhibited. Highly preferred indications include disorders of the musculoskeletal system.	referred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), endocrine disorders (e.g., as described below under "Endocrine
Exemplary assays for PI3 kinase activity that may be used or routinely modified to test PI3 kinase-induced activity of polypeptides of the	invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9)·1101-1110	(1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666	(1999), the contents of each of which are herein incorporated by reference in its entirety. Rat myoblast cells that may be used according to these assays	are publicly available (e.g., through the ATCC). Exemplary rat myoblast cells that may be used according to these assays include L6 cells.	L6 is an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuses to form multinucleated myotubes and striated fibers after culture in differentiation media.

Disorders"), neural disorders	(e.g., as described below under	"Neural Activity and	Neurological Diseases"), blood	disorders (e.g., as described	below under "Immune	Activity", "Cardiovascular	Disorders", and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described	below under "Immune	Activity"), and infection (e.g.,	as described below under	"Infectious Disease"). A	highly preferred indication is	diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g.	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence
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	ssel	ntal		nic-		e.g.,	crosis,		d other	S		ers"	emia,		rine	۷),	irment	y and	npaired	SU	and	ı the	ction		arpal		~·	ferred	/or
etic	neuropathy or blood vessel	blockage), seizures, mental	siness,	nonketotic hyperglycemic-	ma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	sease,	hypertension, stroke, and other	diseases and disorders as		"Cardiovascular Disorders"	section below), dyslipidemia,	ers (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infections	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or
to diab	ıy or bl), seizu	ı, drow	c hypei	ıolar co	cular d	ase, ath	cular di	ion, str	and disc	in the	scular	olow), d	disord	in the	" sectio	ıy, visic	etic ret), ulcers	aling, i	ctious c	as desc	s Disea	pecially	act and	drome	1's cont	onal hig	is obes
(e.g., due to diabetic	europatl	ockage	confusion, drowsiness,	nketoti	hyperosmolar coma,	rdiovas	art dise	microvascular disease,	pertens	seases	described in the	ardiova	ction be	endocrine disorders (as	scribed	sorders	uropath	g., diab	ndness	onnd he	g., infe	sorders	nfection	low, esj	nary tra	tunnel syndrome and	puytre	ı additic	lication
(e	ue	<u> </u>	<u>3</u>	u	hy		he	E	hy	di:	de	<u>ှ</u>	Se	en	de	Ä	ne	<u>.</u>	ild		<u>ق</u>	dis	Ir	be	uri	tur	<u>ה</u>	An	ind
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obesity. Additional highly
weight loss or alternatively,
weight gain. Additional
highly preferred indications are
complications associated with
 insulin resistance.
Additional highly preferred
indications are disorders of the
 musculoskeletal system
including myopathies,
muscular dystrophy, and/or as
described herein.
Additional highly preferred
indications include: myopathy,
atrophy, congestive heart
failure, cachexia, myxomas,
fibromas, congenital
 cardiovascular abnormalities,
 heart disease, cardiac arrest,
heart valve disease, and
vascular disease. Highly
preferred indications include
neoplasms and cancer, such as,
rhabdomyoma,
rhabdosarcoma, stomach,
 esophageal, prostate, and
urinary cancer. Preferred
indications also include breast,
lung, colon, pancreatic, brain,
and liver cancer. Other

				preferred indications include
				benign dysproliferative
				disorders and pre-neoplastic
				conditions, such as,
				hyperplasia, metaplasia, and/or
				dysplasia.
HDPWN93	601	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications
		Signaling Pathway	assays for signal transduction	include asthma, allergy,
		in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
	-	(such as	activation, or apoptosis are	inflammation, and
		eosinophils).	well known in the art and may	inflammatory disorders.
			be used or routinely modified	Additional highly preferred
			to assess the ability of	indications include immune
			polypeptides of the invention	and hematopoietic disorders
			(including antibodies and	(e.g., as described below under
			agonists or antagonists of the	"Immune Activity", and
			invention) to promote or	"Blood-Related Disorders"),
			inhibit cell proliferation,	autoimmune diseases (e.g.,
			activation, and apoptosis.	rheumatoid arthritis, systemic
			Exemplary assays for JNK	lupus erythematosis, Crohn"s
			kinase activity that may be	disease, multiple sclerosis
	-		used or routinely modified to	and/or as described below),
			test JNK kinase-induced	immunodeficiencies (e.g., as
			activity of polypeptides of the	described below). Highly
			invention (including antibodies	preferred indications also
			and agonists or antagonists of	include boosting or inhibiting
			the invention) include the	immune cell proliferation.
			assays disclosed in Forrer et	Preferred indications include
			al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
			1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
			Cell Res 247(2): 495-504	described below under

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"Hyperproliferative	Disorders"). Highly preferred	indications include boosting an	eosinophil-mediated immune	response, and suppressing an	eosinophil-mediated immune	response.																								
(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils.	Eosinophils are important in	the late stage of allergic	reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-
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of Cell		A highly preferred embodiment of the invention
109	induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Kinase assay. JNK and p38 kinase assays for signal
	•	Activation of Endothelial Cell
HDPWN93		601
		HDPWN93

or stimulating endothelial cell	_		ss invention includes a method	of for inhibiting endothelial cell	growth. A highly preferred		on) to includes a method for	stimulating endothelial cell		ays highly preferred embodiment	of the invention includes a	or method for inhibiting	JNK endothelial cell proliferation.	A highly preferred	the embodiment of the invention	odies includes a method for	s of stimulating apoptosis of	endothelial cells. An	et alternative highly preferred	101- embodiment of the invention	Exp includes a method for	inhibiting (e.g., decreasing)	m;)); A highly preferred	embodiment of the invention	and includes a method for	Mol stimulating (e.g., increasing)		ich alternative highly preferred	
-	apoptosis are well known in	the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	promote or inhibit cell	proliferation, activation, and	apoptosis. Exemplary assays	for JNK and p38 kinase	activity that may be used or	routinely modified to test JNK	and p38 kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by
Signaling Pathway.								-																					-	
													-																	

includes a method for	inhibiting (e.g., decreasing) the	activation of and/or	inactivating endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	reguration left ventricular
reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.														
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dysfunction, atherosclerosis	and atheroselerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	
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include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and
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lymphatic disorders such as	Imphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.
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					Additional highly preferred
					indications include fibromas,
					heart disease, cardiac arrest,
					heart valve disease, and
					vascular disease.
					Preferred indications include
				`	blood disorders (e.g., as
					described below under
					"Immune Activity", "Blood-
					Related Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
_	HDPXY01	602	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
				of insulin are well-known in	is diabetes mellitus. An
				the art and may be used or	additional highly preferred
				routinely modified to assess	indication is a complication

the ability of polypeptides of	associated with diabetes (e.g.,
antibodies and agonists or	nephropathy, kidney disease
antagonists of the invention) to	(e.g., renal failure,
stimulate insulin secretion.	nephropathy and/or other
For example, insulin secretion	diseases and disorders as
is measured by FMAT using	described in the "Renal
anti-rat insulin antibodies.	Disorders" section below),
Insulin secretion from	diabetic neuropathy, nerve
pancreatic beta cells is	disease and nerve damage
upregulated by glucose and	(e.g., due to diabetic
also by certain	neuropathy), blood vessel
proteins/peptides, and	blockage, heart disease, stroke,
disregulation is a key	impotence (e.g., due to diabetic
component in diabetes.	neuropathy or blood vessel
Exemplary assays that may be	blockage), seizures, mental
used or routinely modified to	confusion, drowsiness,
test for stimulation of insulin	nonketotic hyperglycemic-
secretion (from pancreatic	hyperosmolar coma,
cells) by polypeptides of the	cardiovascular disease (e.g.,
invention (including antibodies	heart disease, atherosclerosis,
and agonists or antagonists of	microvascular disease,
the invention) include assays	hypertension, stroke, and other
disclosed in: Shimizu, H., et	diseases and disorders as
al., Endocr J, 47(3):261-9	described in the
(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
17 (1999); Filipsson, K., et al.,	endocrine disorders (as
Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
(1998); Olson, L.K., et al., J	Disorders" section below),
Biol Chem, 271(28):16544-52	neuropathy, vision impairment

(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection	(e.g., infectious diseases and disorders as described in the "Infectious Diseases" section	urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or	indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
(1996); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999),	the contents of each of which is herein incorporated by reference in its entirety.	used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated.	Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.

HDTBD53	Assays for muscle cell	ui ux	 routinely modified to assess muscle (such as,	the ability of polypeptides of habdomyoma, and	the invention (including rhabdosarcoma),)r	n) to	stimulate or inhibit myoblast cachexia, myxomas, fibromas,	cell proliferation. Exemplary congenital cardiovascular	proliferation that may be used cardiac arrest, heart valve	or routinely modified to test disease, vascular disease, and	activity of polypeptides and also as described below under	•	(including agonists or stimulating myoblast	ention)	include, for example, assays myoblast proliferation.	 "Possible role for the c-ski	gene in the proliferation of	myogenic cells in regenerating	skeletal muscles of rats" Dev	Growth Differ Apr;43(2):155-	64 (2001); Ewton DZ, et al.,	"IGF binding proteins-4, -5	and -6 may play specialized	roles during L6 myoblast	proliferation and	differentiation! I D. Jamie 1
HDTBD53	603							_																			
	HDTBD53																										

			and, Pampusch MS, et al.,"Effect of transforming	
			growth factor beta on proliferation of L6 and	
			embryonic porcine myogenic	
			cells" J Cell Physiol	
			Jun;143(3):524-8 (1990); the	
			contents of each of which are	•
			herein incorporated by	
			reference in their entirety.	
			Exemplary myoblast cells that	
			may be used according to these	
			assays include the rat myoblast	
			L6 cell line. Rat myoblast L6	
			cells are an adherent rat	
			myoblast cell line, isolated	
			from primary cultures of rat	
			thigh muscle, that fuse to form	
			multinucleated myotubes and	
			striated fibers after culture in	
			differentiation media.	
HDTBV77	604	Regulation of	Assays for the regulation of	A highly preferred indication
		transcription via	transcription through the	is diabetes mellitus.
		DMEF1 response	DMEF1 response element are	Additional highly preferred
-		element in	well-known in the art and may	indications include
		adipocytes and pre-	be used or routinely modified	complications associated with
		adipocytes	to assess the ability of	diabetes (e.g., diabetic
			polypeptides of the invention	retinopathy, diabetic
			(including antibodies and	nephropathy, kidney disease
			agonists or antagonists of the	(e.g., renal failure,
			invention) to activate the	nephropathy and/or other

diseases and disorders as described in the "Renal Disorders" section below),	diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy) blood vessel	blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel	confusion, drowsiness, mental nonketotic hyperglycemic-	hyperosmolar coma, cardiovascular disease (e.g.,	heart disease, atherosclerosis, microvascular disease,	hypertension, stroke, and other diseases and disorders as described in the	"Cardiovascular Disorders" section below), dyslipidemia,	endocrine disorders (as described in the "Endocrine	Disorders" section below), neuropathy, vision impairment	blindness), ulcers and impaired	wound healing, and infection (e.g., infectious diseases and	disorders as described in the
DMEF1 response element in a reporter construct (such as that containing the GLUT4	promoter) and to regulate insulin production. The DMEF1 response element is	present in the OLO 14 promoter and binds to MEF2 transcription factor and another transcription factor that is	of Glut4 expression in skeletal muscle. GLUT4 is the primary	insulin-responsive glucose transporter in fat and muscle	tissue. Exemplary assays that may be used or routinely	modified to test for DMEF1 response element activity (in adipocytes and pre-adipocytes)	by polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include assays	disclosed in Thai, M.V., et al., J Biol Chem, 273(23):14285-92	(1996), Mold, 3., et al., 3 Diol Chem, 275(21):16323-8	(2000); Liu, M.L., et al., J Biol Chem, 269(45):28514-21	(1994); "Identification of a 30-
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"Infectious Diseases" section	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional highly	preferred indications are	complications associated with	insulin resistance.																		
base pair regulatory element and novel DNA binding	protein that regulates the	human GLUT4 promoter in	transgenic mice", J Biol Chem.	2000 Aug 4;275(31):23666-73;	Berger, et al., Gene 66:1-10	(1988); and, Cullen, B., et al.,	Methods in Enzymol.	216:362–368 (1992), the	contents of each of which is	herein incorporated by	reference in its entirety.	Adipocytes and pre-adipocytes	that may be used according to	these assays are publicly	available (e.g., through the	ATCC) and/or may be	routinely generated.	Exemplary cells that may be	used according to these assays	include the mouse 3T3-L1 cell	line which is an adherent	mouse preadipocyte cell line.	Mouse 3T3-L1 cells are a	continuous substrain of 3T3	fibroblasts developed through	clonal isolation. These cells	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation
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			culture conditions.	
Н DТDQ23	909	Endothelial Cell	Caspase Apoptosis. Assays for	A highly preferred
		Apoptosis	caspase apoptosis are well	embodiment of the invention
			known in the art and may be	includes a method for
			used or routinely modified to	stimulating endothelial cell
			assess the ability of	growth. An alternative highly
	-		polypeptides of the invention	preferred embodiment of the
			(including antibodies and	invention includes a method
			agonists or antagonists of the	for inhibiting endothelial cell
			invention) to promote caspase	growth. A highly preferred
			protease-mediated apoptosis.	embodiment of the invention
			Induction of apoptosis in	includes a method for
			endothelial cells supporting the	stimulating endothelial cell
			vasculature of tumors is	proliferation. An alternative
			associated with tumor	highly preferred embodiment
			regression due to loss of tumor	of the invention includes a
			blood supply. Exemplary	method for inhibiting
			assays for caspase apoptosis	endothelial cell proliferation.
			that may be used or routinely	A highly preferred
			modified to test capase	embodiment of the invention
			apoptosis activity of	includes a method for
			polypeptides of the invention	stimulating apoptosis of
			(including antibodies and	endothelial cells. An
			agonists or antagonists of the	alternative highly preferred
			invention) include the assays	embodiment of the invention
			disclosed in Lee et al., FEBS	includes a method for
			Lett 485(2-3): 122-126 (2000);	inhibiting (e.g., decreasing)
			Nor et al., J Vasc Res 37(3):	apoptosis of endothelial cells.
			209-218 (2000); and Karsan	A highly preferred
			and Harlan, J Atheroscler	embodiment of the invention
			Thromb 3(2): 75-80 (1996);	includes a method for

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stimulating angiogenisis. An alternative highly preferred embodiment of the invention	includes a method for inhibiting angiogenesis. A	highly preferred embodiment of the invention includes a	method for reducing cardiac	highly preferred embodiment	of the invention includes a	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	bemodynamic orientond and/or
the contents of each of which are herein incorporated by reference in its entirety.	Endothelial cells that may be used according to these assays	are publicly available (e.g., through commercial sources).	Exemplary endothelial cells	these assays include bovine	aortic endothelial cells	of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.												

as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,
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angiosarcoma, haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly preferred indications also include cancers such as.	prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain liver, and	urinary cancer. Preferred indications include benign	pre-neoplastic conditions, such	as, for example, hyperplasia, metaplasia, and/or dysplasia.	Highly preferred indications also include arterial disease.	such as, atherosclerosis,	hypertension, coronary artery disease, inflammatory	vasculitides, Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphedema; and other	vascular disorders such as	asc	and cancer. Highly
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preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as
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				described below under
				"Immune Activity", "Blood-
				Related Disorders", and/or
				"Cardiovascular Disorders").
				Preferred indications include
				autoimmune diseases (e.g.,
				rheumatoid arthritis, systemic
				lupus erythematosis, multiple
				sclerosis and/or as described
				below) and
				immunodeficiencies (e.g., as
				described below). Additional
				preferred indications include
				inflammation and
				inflammatory disorders (such
				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
				and Crohn's disease), and pain
				management.
НБТВQ23	909	Stimulation of	Assays for measuring calcium	A highly preferred
		Calcium Flux in	flux are well-known in the art	indication is diabetes mellitus.
		pancreatic beta	and may be used or routinely	An additional highly preferred
		cells.	modified to assess the ability	indication is a complication
			of polypeptides of the	associated with diabetes (e.g.,
			invention (including antibodies	diabetic retinopathy, diabetic
			and agonists or antagonists of	nephropathy, kidney disease
			the invention) to mobilize	(e.g., renal failure,
			calcium. For example, the	nephropathy and/or other
			FLPR assay may be used to	diseases and disorders as
			measure influx of calcium.	described in the "Renal

Cells normally have very low	Disorders" section below).
concentrations of cytosolic	
calcium compared to much	disease and nerve damage
higher extracellular calcium.	(e.g., due to diabetic
Extracellular factors can cause	
an influx of calcium, leading to	to blockage, heart disease, stroke,
activation of calcium	impotence (e.g., due to diabetic
responsive signaling pathways	
and alterations in cell	blockage), seizures, mental
functions. Exemplary assays	
that may be used or routinely	nonketotic hyperglycemic-
modified to measure calcium	hyperosmolar coma,
flux by polypeptides of the	cardiovascular disease (e.g.,
invention (including antibodies	es heart disease, atherosclerosis,
 and agonists or antagonists of	f microvascular disease,
the invention) include assays	hypertension, stroke, and other
disclosed in: Satin LS, et al.,	diseases and disorders as
Endocrinology, 136(10):4589-	9- described in the
601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
Endocrinology, 136(7):2960-6	6 section below), dyslipidemia,
(1995); Richardson SB, et al.,	
Biochem J, 288 (Pt 3):847-51	described in the "Endocrine
(1992); and, Meats, JE, et al.,	, Disorders" section below),
Cell Calcium 1989 Nov-	neuropathy, vision impairment
Dec;10(8):535-41 (1989), the	e (e.g., diabetic retinopathy and
 contents of each of which is	blindness), ulcers and impaired
 herein incorporated by	wound healing, and infection
reference in its entirety.	(e.g., infectious diseases and
Pancreatic cells that may be	disorders as described in the
used according to these assays	
are publicly available (e.g.,	below, especially of the

			through the ATCC) and/or	urinary tract and skin), carpal
			may be routinely generated.	tunnel syndrome and
			Exemplary pancreatic cells that	Dupuytren's contracture).
			may be used according to these	An additional highly preferred
			assays include HITT15 Cells.	indication is obesity and/or
			HITT15 are an adherent	complications associated with
			epithelial cell line established	obesity. Additional highly
			from Syrian hamster islet cells	preferred indications include
			transformed with SV40. These	weight loss or alternatively,
			cells express glucagon,	weight gain. Aditional
			somatostatin, and	highly preferred indications are
			glucocorticoid receptors. The	complications associated with
			cells secrete insulin, which is	insulin resistance.
			stimulated by glucose and	
			glucagon and suppressed by	
			somatostatin or	
	-		glucocorticoids. ATTC# CRL-	
			1777 Refs: Lord and	
			Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc.	
			Natl. Acad. Sci. USA 78:	
			4339-4343, 1981.	
HE2DE47	909	Regulation of	Caspase Apoptosis. Assays	A highly preferred
		apoptosis in	for caspase apoptosis are well	indication is diabetes mellitus.
		pancreatic beta	known in the art and may be	An additional highly preferred
		cells.	used or routinely modified to	indication is a complication
			assess the ability of	associated with diabetes (e.g.,
			polypeptides of the invention	diabetic retinopathy, diabetic
			(including antibodies and	nephropathy, kidney disease
			agonists or antagonists of the	(e.g., renal failure,
			invention) to promote caspase	nephropathy and/or other

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discourse and disconfigure	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the
protesse mediated anomores	procease-incurated apoptosis.	Apoptosis in pancreatic beta is	associated with induction and	progression of diabetes.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in: Loweth, AC, et	al., FEBS Lett, 400(3):285-8	(1997); Saini, KS, et al.,	Biochem Mol Biol Int,	39(6):1229-36 (1996);	Krautheim, A., et al., Br J	Pharmacol, 129(4):687-94	(2000); Chandra J, et al.,	Diabetes, 50 Suppl 1:S44-7	(2001); Suk K, et al., J	Immunol, 166(7):4481-9	(2001); Tejedo J, et al., FEBS	Lett, 459(2):238-43 (1999);	Zhang, S., et al., FEBS Lett,	455(3):315-20 (1999); Lee et	al., FEBS Lett 485(2-3): 122-	126 (2000); Nor et al., J Vasc	Res 37(3): 209-218 (2000);	and Karsan and Harlan. I
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			"Intections Inserse as a section
		80 (1006): the contents of each	Letenous Listuacia section
		ov (1990), the contents of each	below, especially of the
		of which are herein	urinary tract and skin), carpal
_		incorporated by reference in its	tunnel syndrome and
		entirety. Pancreatic cells that	Dupuytren's contracture).
		may be used according to these	An additional highly preferred
		assays are publicly available	indication is obesity and/or
		(e.g., through the ATCC)	complications associated with
		and/or may be routinely	obesity. Additional highly
		generated. Exemplary	preferred indications include
		pancreatic cells that may be	weight loss or alternatively,
		used according to these assays	weight gain. Aditional
		include RIN-m. RIN-m is a	highly preferred indications are
	-	rat adherent pancreatic beta	complications associated with
		cell insulinoma cell line	insulin resistance.
		derived from a radiation	
		induced transplantable rat islet	
		cell tumor. The cells produce	
		and secrete islet polypeptide	
-		hormones, and produce insulin,	
		somatostatin, and possibly	
		glucagon. ATTC: #CRL-2057	
		Chick et al. Proc. Natl. Acad.	
		Sci. 1977 74:628; AF et al.	
		Proc. Natl. Acad. Sci. 1980	
		77:3519.	
HE2EB74 607	Activation of	Kinase assay. JNK and p38	A highly preferred
	Endothelial Cell	kinase assays for signal	embodiment of the invention
	p38 or JNK	transduction that regulate cell	includes a method for
	Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
		apoptosis are well known in	growth. An alternative highly

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preferred embodiment of the	invention includes a method	for inhibiting endothelial cell	growth. A highly preferred	embodiment of the invention	includes a method for	stimulating endothelial cell	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	endothelial cell proliferation.	A highly preferred	embodiment of the invention	includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	endothelial cell activation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing) the
the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	promote or inhibit cell	proliferation, activation, and	apoptosis. Exemplary assays	for JNK and p38 kinase	activity that may be used or	routinely modified to test JNK	and p38 kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be
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activation of and/or inactivating endothelial cells. A highly preferred	embodiment of the invention includes a method for	stimulating angiogenisis. An alternative highly preferred	embodiment of the invention includes a method for	inhibiting angiogenesis. A	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	nigniy preferred embodiment of the invention includes a	method for inducing cardiac	hypertrophy. Highly	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular
used according to these assays are publicly available (e.g., through the ATCC).	Exemplary endothelial cells that may be used according to	these assays include human umbilical vein endothelial cells	(HUVEC), which are endothelial cells which line	venous blood vessels, and are	involved in functions usar include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.								WI.						
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intracardiac shunt, cardiac hypetrophy, myocardial infaction, chronic hemodynamic overload, an as described below under "Cardiovascular Disorders" Highly preferred indication include cardiovascular, endothelial and/or angioger disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessel such as diabetes mellitus, as well as diseases of the vessel arteries, capillaries, veins and/or lymphatics). Highly preferred are indications the stimulate angiogenesis and/ cardiovascularization. High preferred are indications the inhibit angiogenesis and/or cardiovascularization. Highly preferred indication include antiangiogenic activ to treat solid tumors, leukemias, and kaposi's sarcoma, and retinal disord such as Kanori's sarcoma, such as Kanori's sarcoma,		disease, diabetic nephropathy,
hypertrophy, myocardial infarction, chronic hemodynamic overload, as described below under "Cardiovascular Disorder "Cardiovascular Disorder Highly preferred indication include cardiovascular. Pinched cardiovascular Disorders (e.g., systemic disorders (e.g., systemic disorders that affect vess such as dispetes mellitus, well as diseases of the verthermselves, such as of the arteries, capillaries, veins and/or lymphatics). High preferred are indications stimulate angiogenesis and cardiovascularization. Highly preferred findication include antiangiogenic and include antiangiogenic and to treat soil dumors, leukemias, and Kaposi"s sarcoma, and retinal disorder enchance and cincidate suricible encoplasms and cincidates as Amori's sarcoma, and retinal disorder enchance and certain discaling include encoplasms and centain describers.		intracardiac shunt, cardiac
infarction, chronic hemodynamic overload, as described below under "Cardiovascular Disorder Highly preferred indication include cardiovascular, endothelial and/or angiog disorders that affect vess such as diabetes mellitus, well as diaseases of the verthermeters, such as of the arteries, capillaries, veins and/or lymphatics). High preferred are indications stimulate angiogenesis and cardiovascularization. Highly preferred are indications inhibit angiogenesis and cardiovascularization. Highly preferred are indications inhibit angiogenesis and cardiovascularization. Highly preferred indication include antiangiogenesis and cardiovascularization. Highly preferred indications inhibit angiogenesis and cardiovascularization. Highly preferred indications include antiangiogenesis and cardiovascularization and cardiovascularization include antiangiogenesis and cardiovascularization and cardiovascula		hypertrophy, myocardial
hemodynamic overload, as described below under "Cardiovascular Disorder Highly preferred indicativine due cardiovascular, include cardiovascular, endothelial and/or angiog disorders that affect vess such as distorative and arteries, capillaries, veins and/or lymphatics). High preferred are indications stimulate angiogenesis and cardiovascularization. High preferred are indications inhibit angiogenesis and cardiovascularization. Highly preferred indications include antangiogenesis at to treat soil dumors, leukemias, and Kaposi"s sarcoma, and retinal disor Highly preferred indicati include neoplasms and cardiovascularization and retinal disor Highly preferred indicati include neoplasms and cardiovascularization and such as Kanosi's sarcoma, and retinal disorder or such as Kanosi's sarcoma, and retinal disorder and a Kanosi's sarcoma, and retinal disorder and and a cardiovascularization.		infarction, chronic
"Cardiovascular Disorder Highly preferred indicatif include cardiovascular, include cardiovascular, endothelial and/or angiog disorders (e.g., systemic disorders that affect vess such as diabetes mellitus, well as diseases of the ve themselves, such as of the ve themselves, such as of the ver and/or lymphatics). High preferred are indications stimulate angiogenesis and/ cardiovascularization. Highly preferred indications inhibit angiogenesis and/ cardiovascularization. Highly preferred indicatif include antangiogenic at to treat soil dumors, leukemias, and Kaposı"s sarcoma, and retinal diso Highly preferred indicatif include neoplasms and cs such as Kanosi's sarcoma, sarcoma, and retinal diso		hemodynamic overload, and/or
"Cardiovascular Disorder Highly preferred indication include cardiovascular, endothelial and/or angiog disorders (e.g., systemic disorders (e.g., systemic disorders that affect vess such as diabetes mellitus, well as diseases of the ventemaches, such as of the arteries, capillaries, veins and/or lymphatics). High preferred are indications stimulate angiogenesis are cardiovascularization. Highly preferred are indications inhibit angiogenesis and/cardiovascularization. Highly preferred indications include antiangrogenic act to treat solid tumors, leukemias, and Kaposi's sarcoma, and retinal disorders include neoplasms and content such as Kanori's sarcoma, and retinal disorders include neoplasms and content such as Kanori's sarcona, such as Canori's sarcona, such as Canori's sarcona, such as Canori's sarcona, such as Canori's sarcona, such as Canoria sarcona, such as Canoria sarcona, such as Canoria sarcona, such as Canoria sarcona, such as Ca		as described below under
Highly preferred indication include cardiovascular, endothelial and/or angiog disorders (e.g., systemic disorders that affect vess such as diabetes mellitus, well as diseases of the vest themselves, such as of the arteries, capillaries, veins and/or lymphatics). High preferred are indications stimulate angiogenesis at cardiovascularization. Highly preferred are indications inhibit angiogenesis and cardiovascularization. Highly preferred indications include antiangiogenic act to treat solid tumors, leukemias, and Kaposi's sacroma, and retinal disordicular include neoplasms and cancel such as Kanosi's sacroma,	 	"Cardiovascular Disorders").
include cardiovascular, endothelial and/or angiog disorders that affect vess such as diabetes mellitus, well as diseases of the ve themselves, such as of thy arteries, capillaries, veins and/or lymphatics). High preferred are indications stimulate angiogenesis ard cardiovascularization. Hi preferred are indications inhibit angiogenesis and/ cardiovascularization. Highly preferred indicati include antiangiogenic ac to treat solid tumors, leukemias, and Kaposi's sarcoma, and retinal disor Highly preferred indicati include neoplasms and curred such as Kanosi's sarcoma,		Highly preferred indications
endothelial and/or angiog disorders (e.g., systemic disorders that affect vesss such as diabetes mellitus, well as diseases of the ve themselves, such as of th arteries, capillaries, veins and/or lymphatics). High preferred are indications stimulate angiogenesis and cardiovascularization. Hi preferred are indications inhibit angiogenesis and/ cardiovascularization. Highly preferred indicati, include antiangiogenic as to treat solid tumors, leukemias, and Kaposi''s sarcoma, and retinal diso Highly preferred indicati, include neoplasms and c, such as Kanosi''s sarcoma, such as Kanosi''s sarcoma, such as Kanosi''s sarcoma, such as Kanosi''s sarcoma,		include cardiovascular,
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disorders that affect vess such as diabetes mellitus, well as diseases of the ve themselves, such as of the arteries, capillaries, veins and/or lymphatics). High preferred are indications simulate angiogenesis at cardiovascularization. High preferred are indications inhibit angiogenesis and cardiovascularization. Highly preferred indication include antiangiogenic at to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal diso Highly preferred indication include neoplasms and casuch as Kanosi's sarcoma such as Kanosi's sarcom		disorders (e.g., systemic
such as diabetes mellitus, well as diseases of the verthemselves, such as of the arteries, capillaries, veins and/or lymphatics). High preferred are indications stimulate angiogenesis are cardiovascularization. High preferred are indications inhibit angiogenesis and cardiovascularization. Highly preferred indication include antiangiogenic at to treat solid tumors, leukemias, and retinal disos sarcoma, and retinal disos Highly preferred indication include neoplasms and capinas sarcoma, such as Kanosi's sarcoma such as Sarcoma such as Kanosi's sarcoma such as Sarcoma suc		disorders that affect vessels
well as diseases of the ve themselves, such as of th arteries, capillaries, veins and/or lymphatics). High preferred are indications stimulate angiogenesis ar cardiovascularization. Hi preferred are indications inhibit angiogenesis and/ cardiovascularization. Highly preferred indication include antiangiogenic at to treat solid tumors, leukemias, and Kaposi''s sarcoma, and retinal diso Highly preferred indicati include neoplasms and oc such as Kanosi''s sarcom		such as diabetes mellitus, as
themselves, such as of the arteries, capillaries, veins and/or lymphatics). High preferred are indications stimulate angiogenesis ar cardiovascularization. Hi preferred are indications inhibit angiogenesis and/cardiovascularization. Highly preferred indicationinclude antiangiogenic acto treat solid tumors, leukemias, and Kaposi''s sarcoma, and retinal diso Highly preferred indicati include neoplasms and consuch as Kaposi''s sarcom		well as diseases of the vessels
arteries, capillaries, veins and/or lymphatics). High preferred are indications stimulate angiogenesis ar cardiovascularization. Hi preferred are indications inhibit angiogenesis and/cardiovascularization. Highly preferred indication include antiangiogenic at to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal diso Highly preferred indicati include neoplasms and cancer such as Kaposi's sarcom		themselves, such as of the
and/or lymphatics). High preferred are indications stimulate angiogenesis ar cardiovascularization. High preferred are indications inhibit angiogenesis and/cardiovascularization. Highly preferred indication include antiangiogenic acto treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal diso Highly preferred indicati include neoplasms and consults as Kanosi"s sarcom		arteries, capillaries, veins
preferred are indications stimulate angiogenesis ar cardiovascularization. Hi preferred are indications inhibit angiogenesis and/cardiovascularization. Highly preferred indication include antiangiogenic at to treat solid tumors, leukemias, and Kaposi's sarcoma, and retinal diso Highly preferred indication include neoplasms and can such as Kanosi's sarcom		and/or lymphatics). Highly
stimulate angiogenesis ar cardiovascularization. Hi preferred are indications inhibit angiogenesis and/cardiovascularization. Highly preferred indication include antiangiogenic acto treat solid tumors, leukemias, and Kaposi's sarcoma, and retinal diso Highly preferred indication include neoplasms and casuch as Kanosi's sarcom		preferred are indications that
cardiovascularization. Hi preferred are indications inhibit angiogenesis and/cardiovascularization. Highly preferred indication include antiangiogenic act to treat solid tumors, leukemias, and Kaposi's sarcoma, and retinal diso Highly preferred indication include neoplasms and consuch as Kanosi's sarcoma.		stimulate angiogenesis and/or
preferred are indications inhibit angiogenesis and/cardiovascularization. Highly preferred indication include antiangiogenic act to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal diso Highly preferred indication include neoplasms and consuch as Kaposi's sarcomes.		cardiovascularization. Highly
inhibit angiogenesis and/cardiovascularization. Highly preferred indication include antiangiogenic act to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal diso Highly preferred indication include neoplasms and cannot be as Kaposi's sarcomes and cannot be as Kaposi's sarcomes.		preferred are indications that
cardiovascularization. Highly preferred indication include antiangiogenic act to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disoo Highly preferred indication include neoplasms and can such as Kaposi"s sarcomes such as Kaposi"s sarcomes such as Kaposi"s sarcomes.		inhibit angiogenesis and/or
Highly preferred indication include antiangiogenic act to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal diso Highly preferred indication include neoplasms and can such as Kaposi"s sarcom		cardiovascularization.
include antiangiogenic ac to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal diso Highly preferred indicati include neoplasms and co		Highly preferred indications
to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal diso Highly preferred indicati include neoplasms and ca		 include antiangiogenic activity
leukemias, and Kaposi"s sarcoma, and retinal diso Highly preferred indication include neoplasms and can such as Kaposi"s sarcom		to treat solid tumors,
Sarcoma, and retinal diso Highly preferred indication include neoplasms and control as Kanosi's sarcom		leukemias, and Kaposi"s
Highly preferred indication include neoplasms and can be such as Kanosi''s sarcom		sarcoma, and retinal disorders.
include neoplasms and call include neoplasms and		Highly preferred indications
Such as Kanosi''s sarcom		include neoplasms and cancer,
Troping a rooder ton trans		such as, Kaposi"s sarcoma,

hemangioma (capillary and	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud's	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,

										•																<i></i>			

lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also	include trauma such as wounds, burns, and injured tissue (e.g., vascular injury	balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring,	ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal	diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke,	graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph	angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis	and related conditions. Additional highly preferred
	•						

heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory bowel disease and Crohn's disease), and pain	nd p38 Preferred indications include al neoplastic diseases (e.g., as described below under on, or "Hyperproliferative own in Disorders"), blood disorders ed or (e.g., as described below under
	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or
	Activation of T-Cell p38 or JNK Signaling Pathway.
	809
·	HE2NV57

	routinely modified to assess	"Immine Activity"
	the obility of walvantides of	"Conditional Discondent
	the double of polypepulies of	Caldiovascular Disolucis,
	guinniaui) iioiiiisaiii aii	alid/of biood-Kelaled
-	antibodies and agonists or	Disorders"), and infection
	antagonists of the invention) to	(e.g., an infectious disease as
	promote or inhibit immune cell	described below under
	(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
	activation, and apoptosis.	preferred indications include
	Exemplary assays for JNK and	autoimmune diseases (e.g.,
	p38 kinase activity that may be	rheumatoid arthritis, systemic
	used or routinely modified to	lupus erythematosis, multiple
	test JNK and p38 kinase-	sclerosis and/or as described
	induced activity of	below) and
	polypeptides of the invention	immunodeficiencies (e.g., as
	(including antibodies and	described below). Additional
	agonists or antagonists of the	highly preferred indications
	invention) include the assays	include inflammation and
	disclosed in Forrer et al., Biol	inflammatory disorders.
	Chem 379(8-9):1101-1110	Highly preferred indications
	(1998); Gupta et al., Exp Cell	also include neoplastic
	Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
	Symp 64:29-48 (1999); Chang	below under
	and Karin, Nature	"Hyperproliferative
	410(6824):37-40 (2001); and	Disorders"). Highly preferred
	Cobb MH, Prog Biophys Mol	indications include neoplasms
	Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
	the contents of each of which	lymphoma, prostate, breast,
	are herein incorporated by	lung, colon, pancreatic,
	reference in its entirety. T	esophageal, stomach, brain,
	cells that may be used	liver, and urinary cancer. Other

				according to these assays are	preferred indications include
				publicly available (e.g.,	benign dysproliferative
				through the ATCC).	disorders and pre-neoplastic
				Exemplary mouse T cells that	conditions, such as, for
				may be used according to these	example, hyperplasia,
				assays include the CTLL cell	metaplasia, and/or dysplasia.
				line, which is an IL-2	Preferred indications include
				dependent suspension-culture	arthritis, asthma, AIDS,
				cell line with cytotoxic	allergy, anemia, pancytopenia,
				activity.	leukopenia, thrombocytopenia,
					Hodgkin"s disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt"s lymphoma,
	•	•			granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
_					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HE2NV57	809	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
				of insulin are well-known in	is diabetes mellitus. An
				the art and may be used or	additional highly preferred
	-			routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
-				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as

		is measured by FMAT using	described in the "Renal
		anti-rat insulin antibodies.	Disorders" section below),
		Insulin secretion from	diabetic neuropathy, nerve
		pancreatic beta cells is	disease and nerve damage
		upregulated by glucose and	(e.g., due to diabetic
		also by certain	neuropathy), blood vessel
		proteins/peptides, and	blockage, heart disease, stroke,
	-	disregulation is a key	impotence (e.g., due to diabetic
		component in diabetes.	neuropathy or blood vessel
-		Exemplary assays that may be	blockage), seizures, mental
-		used or routinely modified to	confusion, drowsiness,
		test for stimulation of insulin	nonketotic hyperglycemic-
		secretion (from pancreatic	hyperosmolar coma,
		cells) by polypeptides of the	cardiovascular disease (e.g.,
	-	invention (including antibodies	heart disease, atherosclerosis,
	,	and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
		disclosed in: Shimizu, H., et	diseases and disorders as
-		al., Endocr J, 47(3):261-9	described in the
		(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
		Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
		17 (1999); Filipsson, K., et al.,	endocrine disorders (as
		Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
		(1998); Olson, L.K., et al., J	Disorders" section below),
		Biol Chem, 271(28):16544-52	neuropathy, vision impairment
		(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
		Journal of Biomolecular	blindness), ulcers and impaired
		Screening, 4:193-204 (1999),	wound healing, and infection
		the contents of each of which	(e.g., infectious diseases and
		is herein incorporated by	disorders as described in the
		reference in its entirety.	"Infectious Diseases" section

			Pancreatic cells that may be	helow especially of the
			used according to these assays	uringry tract and chin) comed
			asea according to these assays	uninaly flact and skilly, calpai
		-	ale publicity available (e.g.,	tunnel syndrome and
			through the ATCC) and/or	Dupuytren's contracture).
			may be routinely generated.	An additional highly preferred
			Exemplary pancreatic cells that	indication is obesity and/or
			may be used according to these	complications associated with
			assays include HITT15 Cells.	obesity. Additional highly
			HITT15 are an adherent	preferred indications include
			epithelial cell line established	weight loss or alternatively,
		-	from Syrian hamster islet cells	weight gain. Additional highly
			transformed with SV40. These	preferred indications are
			cells express glucagon,	complications associated with
			somatostatin, and	insulin resistance.
			glucocorticoid receptors. The	
			cells secrete insulin, which is	
			stimulated by glucose and	
			glucagon and suppressed by	
			somatostatin or	
			glucocorticoids. ATTC# CRL-	
			1777 Refs: Lord and	
_			Ashcroft. Biochem. J. 219:	
		-	547-551; Santerre et al. Proc.	
			Natl. Acad. Sci. USA 78:	
			4339-4343, 1981.	
HE2PH36	609	Regulation of	Assays for the regulation of	A highly preferred indication
		viability and	viability and proliferation of	is diabetes mellitus. An
		proliferation of	cells in vitro are well-known in	additional highly preferred
		pancreatic beta	the art and may be used or	indication is a complication
	_	cells.	routinely modified to assess	associated with diabetes (e.g.,
			the ability of polypeptides of	diabetic retinopathy, diabetic

	the invention (including	nephropathy, kidney disease
	antibodies and agonists or	(e.g., renal failure,
	antagonists of the invention) to	nephropathy and/or other
	regulate viability and	diseases and disorders as
	proliferation of pancreatic beta	described in the "Renal
	cells. For example, the Cell	Disorders" section below),
	Titer-Glo luminescent cell	diabetic neuropathy, nerve
	viability assay measures the	disease and nerve damage
-	number of viable cells in	(e.g., due to diabetic
	culture based on quantitation	neuropathy), blood vessel
	of the ATP present which	blockage, heart disease, stroke,
	signals the presence of	impotence (e.g., due to diabetic
	metabolically active cells.	neuropathy or blood vessel
	Exemplary assays that may be	blockage), seizures, mental
	used or routinely modified to	confusion, drowsiness,
	test regulation of viability and	nonketotic hyperglycemic-
	proliferation of pancreatic beta	hyperosmolar coma,
	cells by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
-	disclosed in: Friedrichsen BN,	diseases and disorders as
	et al., Mol Endocrinol,	described in the
	15(1):136-48 (2001); Huotari	"Cardiovascular Disorders"
	MA, et al., Endocrinology,	section below), dyslipidemia,
	139(4):1494-9 (1998); Hugl	endocrine disorders (as
	SR, et al., J Biol Chem 1998	described in the "Endocrine
	Jul 10;273(28):17771-9	Disorders" section below),
	(1998), the contents of each of	neuropathy, vision impairment
	which is herein incorporated	(e.g., diabetic retinopathy and
	by reference in its entirety.	blindness), ulcers and impaired

			Pancreatic cells that may be	wound healing, and infection
			used according to these assays	(e.g., infectious diseases and
-			are publicly available (e.g.,	disorders as described in the
			through the ATCC) and/or	"Infectious Diseases" section
			may be routinely generated.	below, especially of the
			Exemplary pancreatic cells that	urinary tract and skin), carpal
			may be used according to these	tunnel syndrome and
			assays include rat INS-1 cells.	Dupuytren's contracture). An
			INS-1 cells are a semi-	additional highly preferred
			adherent cell line established	indication is obesity and/or
			from cells isolated from an X-	complications associated with
			ray induced rat transplantable	obesity. Additional highly
			insulinoma. These cells retain	preferred indications include
			characteristics typical of native	weight loss or alternatively,
			pancreatic beta cells including	weight gain. Additional highly
			glucose inducible insulin	preferred indications are
_			secretion. References: Asfari	complications associated with
			et al. Endocrinology 1992	insulin resistance.
			130:167.	
 HE8DS15	610	Activation of	Kinase assay. Kinase assays,	A highly preferred
		Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
		Signaling Pathway	assay, for ERK signal	includes a method for
			transduction that regulate cell	stimulating adipocyte
			proliferation or differentiation	proliferation. An alternative
			are well known in the art and	highly preferred embodiment
			may be used or routinely	of the invention includes a
			modified to assess the ability	method for inhibiting
			of polypeptides of the	adipocyte proliferation. A
			invention (including antibodies	highly preferred embodiment
			and agonists or antagonists of	of the invention includes a
			the invention) to promote or	method for stimulating

	inhibit cell proliferation,	adipocyte differentiation. An
	activation, and differentiation.	alternative highly preferred
	Exemplary assays for ERK	embodiment of the invention
	kinase activity that may be	includes a method for
	used or routinely modified to	inhibiting adipocyte
	test ERK kinase-induced	differentiation. A highly
	activity of polypeptides of the	preferred embodiment of the
	invention (including antibodies	invention includes a method
	and agonists or antagonists of	for stimulating (e.g.,
	the invention) include the	increasing) adipocyte
	assays disclosed in Forrer et	activation. An alternative
	al., Biol Chem 379(8-9):1101-	highly preferred embodiment
	1110 (1998); Le Marchand-	of the invention includes a
-	Brustel Y, Exp Clin	method for inhibiting the
	Endocrinol Diabetes	activation of (e.g., decreasing)
	107(2):126-132 (1999);	and/or inactivating adipocytes.
	Kyriakis JM, Biochem Soc	Highly preferred indications
	Symp 64:29-48 (1999); Chang	include endocrine disorders
	and Karin, Nature	(e.g., as described below under
	410(6824):37-40 (2001); and	"Endocrine Disorders").
	Cobb MH, Prog Biophys Mol	Highly preferred indications
	Biol 71(3-4):479-500 (1999);	also include neoplastic
	the contents of each of which	diseases (e.g., lipomas,
	are herein incorporated by	liposarcomas, and/or as
	reference in its entirety.	described below under
	Mouse adipocyte cells that	"Hyperproliferative
	may be used according to these	Disorders"). Preferred
	assays are publicly available	indications include blood
	(e.g., through the ATCC).	disorders (e.g., hypertension,
	Exemplary mouse adipocyte	congestive heart failure, blood
	cells that may be used	vessel blockage, heart disease.

	according to these assays	stroke, impotence and/or as
	include 313-L1 cells. 313-L1	described below under "Immine Activity"
	nreadinocyte cell line that is a	"Cardiovascular Disorders"
	continuous substrain of 3T3	and/or "Blood-Related
	fibroblast cells developed	Disorders"), immune disorders
	through clonal isolation and	(e.g., as described below under
	undergo a pre-adipocyte to	"Immune Activity"), neural
	adipose-like conversion under	disorders (e.g., as described
	appropriate differentiation	below under "Neural Activity
	conditions known in the art.	and Neurological Diseases"),
		and infection (e.g., as
		described below under
		"Infectious Disease").
		A highly preferred indication
		is diabetes mellitus. An
		additional highly preferred
		indication is a complication
		associated with diabetes (e.g.,
		diabetic retinopathy, diabetic
		nephropathy, kidney disease
		(e.g., renal failure,
		nephropathy and/or other
		diseases and disorders as
-		described in the "Renal
		Disorders" section below),
		diabetic neuropathy, nerve
		disease and nerve damage
		(e.g., due to diabetic
		neuropathy), blood vessel
		blockage, heart disease, stroke,

impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	
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												_			-															

<u>.</u>	weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with	insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.	Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred	indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications
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					liposarcomas. Other preferred
_	-				indications include benign
					dysproliferative disorders and
_					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
HE	HE8DS15	610	Regulation of	Assays for the regulation of	A highly preferred
			transcription of	transcription of Malic Enzyme	indication is diabetes mellitus.
			Malic Enzyme in	are well-known in the art and	An additional highly preferred
-			adipocytes	may be used or routinely	indication is a complication
				modified to assess the ability	associated with diabetes (e.g.,
				of polypeptides of the	diabetic retinopathy, diabetic
				invention (including antibodies	nephropathy, kidney disease
				and agonists or antagonists of	(e.g., renal failure,
·				the invention) to regulate	nephropathy and/or other
	-			transcription of Malic Enzyme,	diseases and disorders as
				a key enzyme in lipogenesis.	described in the "Renal
	•			Malic enzyme is involved in	Disorders" section below),
_		_		lipogenesisand its expression is	diabetic neuropathy, nerve
				stimulted by insulin. ME	disease and nerve damage
	_			promoter contains two direct	(e.g., due to diabetic
-				repeat (DR1)- like elements	neuropathy), blood vessel
				MEp and MEd identified as	blockage, heart disease, stroke,
				putative PPAR response	impotence (e.g., due to diabetic
				elements. ME promoter may	neuropathy or blood vessel
				also responds to AP1 and other	blockage), seizures, mental
				transcription factors.	confusion, drowsiness,
-				Exemplary assays that may be	nonketotic hyperglycemic-
				used or routinely modified to	hyperosmolar coma,
_				test for regulation of	cardiovascular disease (e.g.,
				transcription of Malic Enzyme	heart disease, atherosclerosis,

	(in adinopovtes) by	microvascular disease.	
	polypeptides of the invention		
	(including antibodies and		
	agonists or antagonists of the		
	invention) include assays	"Cardiovascular Disorders"	
	disclosed in: Streeper, R.S., et		
	al., Mol Endocrinol,		
	12(11):1778-91 (1998);	described in the "Endocrine	
	Garcia-Jimenez, C., et al., Mol	ol Disorders" section below),	
	Endocrinol, 8(10):1361-9	neuropathy, vision impairment	
	(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and	
	Biol Chem, 274(25):17997-		
	8004 (1999); Ijpenberg, A., et	t wound healing, and infection	
	al., J Biol Chem,	_	
	272(32):20108-20117 (1997);		
	Berger, et al., Gene 66:1-10	"Infectious Diseases" section	
	(1988); and, Cullen, B., et al.,		
	Methods in Enzymol.	urinary tract and skin), carpal	
	216:362–368 (1992), the	tunnel syndrome and	
_	contents of each of which is	Dupuytren's contracture).	
	herein incorporated by	An additional highly preferred	
	reference in its entirety.	indication is obesity and/or	
	Hepatocytes that may be used		
	according to these assays are	obesity. Additional highly	
	publicly available (e.g.,	preferred indications include	
	through the ATCC) and/or	weight loss or alternatively,	
	may be routinely generated.	weight gain. Aditional	
-	Exemplary hepatocytes that	highly preferred indications are	
	may be used according to these	se complications associated with	
	assays includes the H4IIE rat	t insulin resistance.	
	liver hepatoma cell line.		

																					A preferred embodiment of	the invention includes a	method for inhibiting (e.g.,	reducing) TNF alpha	production. An alternative	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) TNF alpha	
Reporter Assay: construct	contains regulatory and coding	sequence of squalene	synthetase, the first specific	enzyme in the cholesterol	biosynthetic pathway. See	Jiang, et al., J. Biol. Chem.	268:12818-128241(993), the	contents of which are herein	incorporated by reference in its	entirety. Cells were treated	with SID supernatants, and	SEAP activity was measured	after 72 hours. HepG2 is a	human hepatocellular	carcinoma cell line (ATCC	HB-8065). See Knowles et al.,	Science. 209:497-9 (1980), the	contents of which are herein	incorporated by reference in its	entirety.	Assays for the activation of	transcription through the	Serum Response Element	(SRE) are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to
Inhibition of	squalene synthetase	gene transcription.									-										Activation of	transcription	through serum	response element in	immune cells (such	as T-cells).				
610																					611									
HE8DS15				_																	HE9CP41									
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indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn's disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,
regulate the serum response	factors and modulate the	expression of genes involved	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2
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highly preferred indications include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,
dependent suspension culture of T cells with cytotoxic	activity.								-																				
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s co disco di live di co					diabetes mellitus, endocarditis,
4 Activation of transcription through the transcription through GAS (Damma Interferon Activation of response element in immune cells (such as T-cells). Activation of Assays for the activation of transcription through the incommune cells (such are well-known in the art and un as T-cells). May be used or routinely Dipmodified to assess the ability into of polypeptides of the invention (including antibodies exand agonists or antagonists of the invention) to regulate Branch involved in a wide variety of me cell functions. Exemplary assays for transcription factors and through the GAS response element activity of polypeptides of the invention (including antibodies exand agonists or antagonists of me					meningitis, Lyme Disease, cardiac reperfusion injury, and
4 Activation of transcription through the transcription through GAS transcription transcription through the transcription transcription transcription transcription transcription transcription transcription transcription transcription are well-known in the art and un may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies exand agonists or antagonists of the invention) to regulate Bastranscription factors and modulate gene expression modulate gene expression modulate gene expression furvough the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies exand agonists or antagonists of madagonists or antagonists of madagonists or antagonists of maganists or antagonists or maganists or antagonists or maganists or antagonists or maganists or antagonists or maganists or antagonists of maganists or antagonists or antagonist and antagonists or antagonists or antagonists and antagonists and antagonist and antagonists and antagonists and antagonists and antagonists and antagonists and antag		-			asthma and allergy. An
distribution of transcription through the inchrough GAS transcription through GAS response element in immune cells (such as T-cells). The invention (including antibodies example and agonists or antagonists of the invention) to regulate STAT transcription factors and involved in a wide variety of modulate gene expression involved in a wide variety of modulate gene expression involved in a wide variety of minvolved in a wide variety of minvolved in a wide variety of minvolved in a wide variety of assays for transcription estimated involved in a wide variety of involving antibodies examples of the involved in a wide variety of involved in a wide variety of involved in a wide variety of involving antibodies examples of the involved in a wide variety of involved invol					additional preferred indication
distribution of transcription of transcription of transcription transcription transcription transcription transcription transcription transcription transcription damped for transcription transcription transcription defends of the immune cells (such are well-known in the art and un as T-cells). May be used or routinely in may be used or routinely in modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the involved in a wide variety of me cell functions. Exemplary assays for transcription factors and through the GAS response lement that may be used or routinely modified to test of polypeptides of the invention (including antibodies examplas and agonists or antagonists of me					is infection (e.g., an infectious
transcription through the inchrough GAS transcription through the inchrough GAS response element in Site (GAS) response element an immune cells (such are well-known in the art and un as T-cells). may be used or routinely incolpypeptides of the invention (including antibodies and agonists or antagonists of (c. the invention) to regulate Bt STAT transcription factors and modulate gene expression involved in a wide variety of me cell functions. Exemplary assays for transcription factors and through the GAS response element that may be used or routinely modified to test be GAS-response element activity disofpolypeptides of the invention (including antibodies example and agonists or antagonists of me					disease as described below
transcription transcription through the transcription through GAS Gamma Interferon Activation (c. franscription response element in site (GAS) response element an immune cells (such are well-known in the art and as T-cells). may be used or routinely Di may be used or routinely in of polypeptides of the invention (including antibodies examed agonists or antagonists of (c. the invention) to regulate Buston involved in a wide variety of modulate gene expression involved in a wide variety of the involution and involved in a wide variety of the involution that may be used or performed in the invention (including antibodies examplary assays for transcription fest of GAS-response element activity disording antibodies exampla and agonists or antagonists of mediand agonists or antagonists of agonists of ago					under "Infectious Disease").
transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of	HE9DG49	612	Activation of	Assays for the activation of	Highly preferred indications
Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of			transcription	transcription through the	include neoplastic diseases
Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of			response element in	Site (GAS) response element	and/or as described below
may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of			immune cells (such	are well-known in the art and	under "Hyperproliferative
			as T-cells).	may be used or routinely	Disorders"). Highly preferred
				modified to assess the ability	indications include neoplasms
				of polypeptides of the	and cancers, such as, for
				invention (including antibodies	example, leukemia, lymphoma
				and agonists or antagonists of	(e.g., T cell lymphoma,
				the invention) to regulate	Burkitt's lymphoma, non-
				STAT transcription factors and	Hodgkins lymphoma,
				modulate gene expression	Hodgkin"s disease),
				involved in a wide variety of	melanoma, and prostate,
				cell functions. Exemplary	breast, lung, colon, pancreatic,
				assays for transcription	esophageal, stomach, brain,
				through the GAS response	liver and urinary cancer. Other
				element that may be used or	preferred indications include
				routinely modified to test	benign dysproliferative
				GAS-response element activity	disorders and pre-neoplastic
				of polypeptides of the	conditions, such as, for
				invention (including antibodies	example, hyperplasia,
l				and agonists or antagonists of	metaplasia, and/or dysplasia.

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Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis
the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary mouse T cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary T cells that may be	used according to these assays	include the CTLL cell line,	which is a suspension culture	of IL-2 dependent cytotoxic T	cells.							
					-		-		-																	7				
																							-						-	

·				Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and
НЕ9НҮ07	613	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation.	asthma and allergy. A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred

	Exemplary assays for ERK	embodiment of the invention
-	kinase activity that may be	includes a method for
	used or routinely modified to	inhibiting adinocyte
	test ERK kinase-induced	differentiation. A highly
	activity of polypeptides of the	dime
	invention (including antibodies	invention includes a method
	and agonists or antagonists of	for stimulating (e.g.,
	the invention) include the	increasing) adipocyte
_	assays disclosed in Forrer et	activation. An alternative
	al., Biol Chem 379(8-9):1101-	highly preferred embodiment
	1110 (1998); Le Marchand-	of the invention includes a
	Brustel Y, Exp Clin	method for inhibiting the
	Endocrinol Diabetes	activation of (e.g., decreasing)
	107(2):126-132 (1999);	and/or inactivating adipocytes.
	Kyriakis JM, Biochem Soc	Highly preferred indications
	Symp 64:29-48 (1999); Chang	include endocrine disorders
	and Karin, Nature	(e.g., as described below under
	410(6824):37-40 (2001); and	"Endocrine Disorders").
	Cobb MH, Prog Biophys Mol	Highly preferred indications
	Biol 71(3-4):479-500 (1999);	also include neoplastic
	the contents of each of which	diseases (e.g., lipomas,
	are herein incorporated by	liposarcomas, and/or as
	reference in its entirety.	described below under
	Mouse adipocyte cells that	"Hyperproliferative
	may be used according to these	Disorders"). Preferred
	assays are publicly available	indications include blood
	(e.g., through the ATCC).	disorders (e.g., hypertension,
	Exemplary mouse adipocyte	congestive heart failure, blood
	cells that may be used	vessel blockage, heart disease,
	according to these assays	stroke, impotence and/or as
	include 3T3-L1 cells. 3T3-L1	described below under

is an adherent mouse	"Immine Activity"
is an adjicion illouse	minimic Activity,
preadipocyte cell line that is a	"Cardiovascular Disorders",
continuous substrain of 3T3	and/or "Blood-Related
fibroblast cells developed	Disorders"), immune disorders
through clonal isolation and	(e.g., as described below under
undergo a pre-adipocyte to	"Immune Activity"), neural
adipose-like conversion under	disorders (e.g., as described
appropriate differentiation	below under "Neural Activity
conditions known in the art.	and Neurological Diseases"),
	and infection (e.g., as
	described below under
	"Infectious Disease").
	A highly preferred indication
	is diabetes mellitus. An
	additional highly preferred
	indication is a complication
	associated with diabetes (e.g.,
	diabetic retinopathy, diabetic
	nephropathy, kidney disease
	(e.g., renal failure,
	nephropathy and/or other
	diseases and disorders as
	described in the "Renal
	Disorders" section below),
	diabetic neuropathy, nerve
	disease and nerve damage
	(e.g., due to diabetic
	neuropathy), blood vessel
	blockage, heart disease, stroke,
	impotence (e.g., due to diabetic
	neuropathy or blood vessel

blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional
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highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the	musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include,	hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as,	lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred

					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
	HE9HY07	613	Regulation of	Assays for the regulation of	A highly preferred
			transcription	transcription through the FAS	indication is diabetes mellitus.
			through the FAS	promoter element are well-	An additional highly preferred
			promoter element	known in the art and may be	indication is a complication
			in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
				assess the ability of	diabetic retinopathy, diabetic
				polypeptides of the invention	nephropathy, kidney disease
				(including antibodies and	(e.g., renal failure,
				agonists or antagonists of the	nephropathy and/or other
•				invention) to activate the FAS	diseases and disorders as
				promoter element in a reporter	described in the "Renal
				construct and to regulate	Disorders" section below),
				transcription of FAS, a key	diabetic neuropathy, nerve
	_			enzyme for lipogenesis. FAS	disease and nerve damage
				promoter is regulated by many	(e.g., due to diabetic
				transcription factors including	neuropathy), blood vessel
				SREBP. Insulin increases FAS	blockage, heart disease, stroke,
				gene transcription in livers of	impotence (e.g., due to diabetic
				diabetic mice. This	neuropathy or blood vessel
				stimulation of transcription is	blockage), seizures, mental
				also somewhat glucose	confusion, drowsiness,
				dependent. Exemplary assays	nonketotic hyperglycemic-
				that may be used or routinely	hyperosmolar coma,
				modified to test for FAS	cardiovascular disease (e.g.,
				promoter element activity (in	heart disease, atherosclerosis,
				hepatocytes) by polypeptides	microvascular disease,
				of the invention (including	hypertension, stroke, and other

			antibodies and agonists or	diseases and disorders as
 			antagonists of the invention)	described in the
 _			include assays disclosed in	"Cardiovascular Disorders"
			Xiong, S., et al., Proc Natl	section below), dyslipidemia,
			Acad Sci U.S.A., 97(8):3948-	endocrine disorders (as
			53 (2000); Roder, K., et al.,	described in the "Endocrine
			Eur J Biochem, 260(3):743-51	Disorders" section below),
			(1999); Oskouian B, et al.,	neuropathy, vision impairment
			Biochem J, 317 (Pt 1):257-65	(e.g., diabetic retinopathy and
			(1996); Berger, et al., Gene	blindness), ulcers and impaired
			66:1-10 (1988); and, Cullen,	wound healing, and infection
			B., et al., Methods in Enzymol.	(e.g., infectious diseases and
			216:362–368 (1992), the	disorders as described in the
			contents of each of which is	"Infectious Diseases" section
			herein incorporated by	below, especially of the
			reference in its entirety.	urinary tract and skin), carpal
			Hepatocytes that may be used	tunnel syndrome and
			according to these assays, such	Dupuytren's contracture).
			as H4IIE cells, are publicly	An additional highly preferred
			available (e.g., through the	indication is obesity and/or
			ATCC) and/or may be	complications associated with
			routinely generated.	obesity. Additional highly
			Exemplary hepatocytes that	preferred indications include
 			may be used according to these	weight loss or alternatively,
			assays include rat liver	weight gain. Aditional
			hepatoma cell line(s) inducible	highly preferred indications are
			with glucocorticoids, insulin,	complications associated with
			or cAMP derivatives.	insulin resistance.
HEBEJ18	614	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
 		Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
		Signaling Pathway.	transduction that regulate cell	described below under

	proliferation, activation, or	"Hyperproliferative
	apoptosis are well known in	Disorders"), blood disorders
	the art and may be used or	(e.g., as described below under
	routinely modified to assess	"Immune Activity",
	the ability of polypeptides of	"Cardiovascular Disorders",
	the invention (including	and/or "Blood-Related
	antibodies and agonists or	Disorders"), and infection
	antagonists of the invention) to	(e.g., an infectious disease as
	promote or inhibit immune cell	described below under
	(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
-	activation, and apoptosis.	preferred indications include
	Exemplary assays for JNK and	autoimmune diseases (e.g.,
	p38 kinase activity that may be	rheumatoid arthritis, systemic
	used or routinely modified to	lupus erythematosis, multiple
	test JNK and p38 kinase-	sclerosis and/or as described
	induced activity of	below) and
	polypeptides of the invention	immunodeficiencies (e.g., as
	 (including antibodies and	described below). Additional
	agonists or antagonists of the	highly preferred indications
	invention) include the assays	include inflammation and
_	disclosed in Forrer et al., Biol	inflammatory disorders.
	Chem 379(8-9):1101-1110	Highly preferred indications
	(1998); Gupta et al., Exp Cell	also include neoplastic
	Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
	Symp 64:29-48 (1999); Chang	below under
	and Karin, Nature	"Hyperproliferative
	 410(6824):37-40 (2001); and	Disorders"). Highly preferred
	Cobb MH, Prog Biophys Mol	indications include neoplasms
	 Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
	the contents of each of which	lymphoma, prostate, breast,

	-			are herein incorporated by	lung, colon, pancreatic,
				reference in its entirety. T	esophageal, stomach, brain,
				cells that may be used	liver, and urinary cancer. Other
				according to these assays are	preferred indications include
				publicly available (e.g.,	benign dysproliferative
				through the ATCC).	disorders and pre-neoplastic
				Exemplary mouse T cells that	conditions, such as, for
				may be used according to these	example, hyperplasia,
				assays include the CTLL cell	metaplasia, and/or dysplasia.
				line, which is an IL-2	Preferred indications include
				dependent suspension-culture	arthritis, asthma, AIDS,
				cell line with cytotoxic	allergy, anemia, pancytopenia,
				activity.	leukopenia, thrombocytopenia,
					Hodgkin"s disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt"s lymphoma,
_					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HEEAQ11	615	Regulation of	Assays for the regulation (i.e.	Highly preferred indications
			viability or	increases or decreases) of	include eosinophilia, asthma,
			proliferation of	viability and proliferation of	allergy, hypersensitivity
			immune cells (such	cells in vitro are well-known in	reactions, inflammation, and
			as human	the art and may be used or	inflammatory disorders.
			eosinophil EOL-1	routinely modified to assess	Additional highly preferred
			cells).	the ability of polypeptides of	indications include immune

			the invention (including	and hematopoietic disorders
•			antibodies and agonists or	(e.g., as described below under
			antagonists of the invention) to	"Immune Activity", and
			regulate viability and	"Blood-Related Disorders"),
			proliferation of eosinophil cells	autoimmune diseases (e.g.,
			and cell lines. For example,	rheumatoid arthritis, systemic
			the CellTiter-Gloô	lupus erythematosis, Crohn"s
			Luminescent Cell Viability	disease, multiple sclerosis
			Assay (Promega Corp.,	and/or as described below),
	·		Madison, WI, USA) can be	immunodeficiencies (e.g., as
			used to measure the number of	described below). Highly
			viable cells in culture based on	preferred indications also
			quantitation of the ATP	include boosting or inhibiting
			present which signals the	immune cell proliferation.
			presence of metabolically	Preferred indications include
			active cells. Eosinophils are a	neoplastic diseases (e.g.,
			type of immune cell important	leukemia, lymphoma, and/or as
			in allergic responses; they are	described below under
			recruited to tissues and	"Hyperproliferative
			mediate the inflammtory	Disorders"). Highly preferred
			response of late stage allergic	indications include boosting an
			reaction. Eosinophil cell lines	eosinophil-mediated immune
			that may be used according to	response, and suppressing an
			these assays are publicly	eosinophil-mediated immune
			available and/or may be	response.
			routinely generated.	
			Exemplary eosinophil cells	
			that may be used according to	
			these assays include EOL-1	
			Cells.	
HEEAQ11	615	Activation of T-	Kinase assay. JNK and p38	Preferred indications include

Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
Signaling Pathway.	transduction that regulate cell	described below under
	proliferation, activation, or	"Hyperproliferative
	apoptosis are well known in	Disorders"), blood disorders
	the art and may be used or	(e.g., as described below under
	routinely modified to assess	"Immune Activity",
	the ability of polypeptides of	"Cardiovascular Disorders",
	the invention (including	and/or "Blood-Related
	antibodies and agonists or	Disorders"), and infection
	antagonists of the invention) to	(e.g., an infectious disease as
	promote or inhibit immune cell	described below under
	(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
	activation, and apoptosis.	preferred indications include
	Exemplary assays for JNK and	autoimmune diseases (e.g.,
	p38 kinase activity that may be	rheumatoid arthritis, systemic
	used or routinely modified to	lupus erythematosis, multiple
	test JNK and p38 kinase-	sclerosis and/or as described
	induced activity of	below) and
	polypeptides of the invention	immunodeficiencies (e.g., as
	(including antibodies and	described below). Additional
	agonists or antagonists of the	highly preferred indications
	invention) include the assays	include inflammation and
	disclosed in Forrer et al., Biol	inflammatory disorders.
	Chem 379(8-9):1101-1110	Highly preferred indications
	(1998); Gupta et al., Exp Cell	also include neoplastic
	Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
	Symp 64:29-48 (1999); Chang	below under
	and Karin, Nature	"Hyperproliferative
-	410(6824):37-40 (2001); and	Disorders"). Highly preferred
	Cobb MH, Prog Biophys Mol	indications include neoplasms

				Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
		<u> </u>		the contents of each of which	lymphoma, prostate, breast,
_				are herein incorporated by	lung, colon, pancreatic,
				reference in its entirety. T	esophageal, stomach, brain,
				cells that may be used	liver, and urinary cancer. Other
				according to these assays are	preferred indications include
				publicly available (e.g.,	benign dysproliferative
				through the ATCC).	disorders and pre-neoplastic
				Exemplary mouse T cells that	conditions, such as, for
				may be used according to these	example, hyperplasia,
_				assays include the CTLL cell	metaplasia, and/or dysplasia.
				line, which is an IL-2	Preferred indications include
				dependent suspension-culture	arthritis, asthma, AIDS,
				cell line with cytotoxic	allergy, anemia, pancytopenia,
		-		activity.	leukopenia, thrombocytopenia,
		_			Hodgkin"s disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt"s lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
	0711 Duit				meningitis, and Lyme Disease.
	HEGAH43	919	Endothelial Cell	Caspase Apoptosis. Assays for	A highly preferred
			Apoptosis	caspase apoptosis are well	embodiment of the invention
				known in the art and may be	includes a method for
				used or routinely modified to	stimulating endothelial cell
				assess the ability of	growth. An alternative highly

preferred embodiment of the invention includes a method for inhibiting endothelial cell	growth. A highly preferred	embodiment of the invention	includes a method for	stimulating endothelial cell	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	endothelial cell proliferation.	A highly preferred	embodiment of the invention	includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment
polypeptides of the invention (including antibodies and	invention) to promote caspase	protease-mediated apoptosis.	Induction of apoptosis in	endothelial cells supporting the	vasculature of tumors is	associated with tumor	regression due to loss of tumor	blood supply. Exemplary	assays for caspase apoptosis	that may be used or routinely	modified to test capase	apoptosis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Lee et al., FEBS	Lett 485(2-3): 122-126 (2000);	Nor et al., J Vasc Res 37(3):	209-218 (2000); and Karsan	and Harlan, J Atheroscler	Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,
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of the invention includes a method for reducing cardiac hypertrophy. An alternative highly preferred embodiment		preferred indications include neoplastic diseases (e.g., as described below under	"Hyperproliferative Disorders"), and disorders of the cardiovascular system	 aortic stenosis, cardiomyopathy, valvular	regurgitation, left ventricular dysfunction atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy, intracardiac shunt, cardiac	hypertrophy, myocardial infarction, chronic	hemodynamic overload, and/or	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic
through commercial sources). Exemplary endothelial cells that may be used according to these assays include bovine	aortic endothelial cells (bAEC), which are an example of endothelial cells which line	in functions that include, but are not limited to,	angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.											

disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins	and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly	preterred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications	include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders.	Highly preferred indications include neoplasms and cancer, such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors,	telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma,	haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as,

prostate, breast, lung, colon, pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and
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atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e. g.,
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include autoimmune diseases	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,
activity of the polypeptides of the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.				
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lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication	is infection (e.g., an infectious
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					under "Infectious Disease").
	HEOMO63	618	Stimulation of	Assays for measuring secretion	A highly preferred
			insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
			from pancreatic	the art and may be used or	An additional highly preferred
_			beta cells.	routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
		_		Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
				upregulated by glucose and	(e.g., due to diabetic
				also by certain	neuropathy), blood vessel
				proteins/peptides, and	blockage, heart disease, stroke,
				disregulation is a key	impotence (e.g., due to diabetic
				component in diabetes.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
				test for stimulation of insulin	nonketotic hyperglycemic-
				secretion (from pancreatic	hyperosmolar coma,
				cells) by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,
				the invention) include assays	hypertension, stroke, and other
				disclosed in: Ahren, B., et al.,	diseases and disorders as
				Am J Physiol, 277(4 Pt	described in the
				2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"

			al Endocrinology.	section below), dyslipidemia,
			138(9):3735-40 (1997); Kim.	endocrine disorders (as
			K.H., et al., FEBS Lett,	described in the "Endocrine
			377(2):237-9 (1995); and,	Disorders" section below),
			Miraglia S et. al., Journal of	neuropathy, vision impairment
			Biomolecular Screening,	(e.g., diabetic retinopathy and
			4:193-204 (1999), the contents	blindness), ulcers and impaired
			of each of which is herein	wound healing, and infection
			incorporated by reference in its	(e.g., infectious diseases and
			entirety. Pancreatic cells that	disorders as described in the
			may be used according to these	"Infectious Diseases" section
			assays are publicly available	below, especially of the
			(e.g., through the ATCC)	urinary tract and skin), carpal
			and/or may be routinely	tunnel syndrome and
			generated. Exemplary	Dupuytren's contracture).
			pancreatic cells that may be	An additional highly preferred
		٠	used according to these assays	indication is obesity and/or
			include rat INS-1 cells. INS-1	complications associated with
			cells are a semi-adherent cell	obesity. Additional highly
			line established from cells	preferred indications include
			isolated from an X-ray induced	weight loss or alternatively,
			rat transplantable insulinoma.	weight gain. Aditional
			These cells retain	highly preferred indications are
			characteristics typical of native	complications associated with
	_		pancreatic beta cells including	insulin resistance.
			glucose inducible insulin	
			secretion. References: Asfari	
			et al. Endocrinology 1992	
			130:167.	
HEPAA46	619	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a

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method for innibiting (e.g., reducing) TNF alpha	production. An alternative	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) TNF alpha	production. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid
Serum Kesponse Element (SRF) are well-known in the		ssess	٠.		antibodies and agonists or	n) to		factors and modulate the	expression of genes involved		for transcription through the		SRE				antagonists of the invention)		Berger et al., Gene 66:1-10		362-	al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and		12(2):105-117 (1997), the	content of each of which are		reference in its entirety. T
through serum	immine cells (such	as T-cells).																											
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arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,
cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.					***															
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arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention
dis distriction of the control of th	stinc em linc of of of additional and additional additional and additional additi
	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK
	Activation of Adipocyte ERK Signaling Pathway
	620
	HEPAB80

includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method	for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment	of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes.	Highly preferred indications include endocrine disorders	"Endocrine Disorders"). Highly preferred indications also include neoplastic diseases (e.g., lipomas,	liposarcomas, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include blood	disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as described below under "Immune Activity",
kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes	Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang	410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which	are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available.	(e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse

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"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental
nreadinocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.																							-
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confusion, drowsiness,	nonketotic nypergryceniic- hynerosmolar coma	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are
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thin bearings against with	insulin resistance	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	lymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred	indications include melanoma,	prostate, lung, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer.	Highly preferred indications	include lipomas and	liposarcomas. Other preferred	indications include benign	dysproliferative disorders and
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				pre-neoplastic conditions, such
				as, for example, hyperplasia,
HEPAB80	620	Regulation of	Assavs for the regulation of	metaplasia, and/or dysplasia.
	,	viability and	viability and proliferation of	is dispates mallitus An
		proliferation of	cells in vitro are well-known in	additional highly preferred
		pancreatic beta	the art and may be used or	indication is a complication
		cells.	routinely modified to assess	associated with diabetes (e.g.
			the ability of polypeptides of	diabetic retinopathy, diabetic
			the invention (including	nephropathy, kidney disease
			antibodies and agonists or	(e.g., renal failure,
			antagonists of the invention) to	nephropathy and/or other
			regulate viability and	diseases and disorders as
			proliferation of pancreatic beta	described in the "Renal
			cells. For example, the Cell	Disorders" section below),
			Titer-Glo luminescent cell	diabetic neuropathy, nerve
			viability assay measures the	disease and nerve damage
			number of viable cells in	(e.g., due to diabetic
			culture based on quantitation	neuropathy), blood vessel
			of the ATP present which	blockage, heart disease, stroke,
	,		signals the presence of	impotence (e.g., due to diabetic
			metabolically active cells.	neuropathy or blood vessel
			Exemplary assays that may be	blockage), seizures, mental
			used or routinely modified to	confusion, drowsiness,
			test regulation of viability and	nonketotic hyperglycemic-
			proliferation of pancreatic beta	hyperosmolar coma,
			cells by polypeptides of the	cardiovascular disease (e.g.,
	_		invention (including antibodies	heart disease, atherosclerosis,
			and agonists or antagonists of	microvascular disease,
	•		the invention) include assays	hypertension, stroke, and other
			disclosed in: Ohtani KI, et al.,	diseases and disorders as

	Endocrinology 139(1):172-8	decoribed in the
	(1000) 17 (1):1/2-0	מכארווות וווי וווי וווי וווי וווי וווי
	(1998); Krautheim A, et al,	"Cardiovascular Disorders"
	Exp Clin Endocrinol Diabetes,	section below), dyslipidemia,
	107 (1):29-34 (1999), the	endocrine disorders (as
	contents of each of which is	described in the "Endocrine
	herein incorporated by	Disorders" section below),
	reference in its entirety.	neuropathy, vision impairment
	Pancreatic cells that may be	(e.g., diabetic retinopathy and
	used according to these assays	blindness), ulcers and impaired
	are publicly available (e.g.,	wound healing, and infection
	through the ATCC) and/or	(e.g., infectious diseases and
	may be routinely generated.	disorders as described in the
	Exemplary pancreatic cells that	"Infectious Diseases" section
	may be used according to these	below, especially of the
	assays include HITT15 Cells.	urinary tract and skin), carpal
	HITT15 are an adherent	tunnel syndrome and
-	epithelial cell line established	Dupuytren's contracture). An
	from Syrian hamster islet cells	additional highly preferred
	transformed with SV40. These	indication is obesity and/or
-	cells express glucagon,	complications associated with
	somatostatin, and	obesity. Additional highly
	glucocorticoid receptors. The	preferred indications include
	cells secrete insulin, which is	weight loss or alternatively,
	stimulated by glucose and	weight gain. Additional highly
	glucagon and suppressed by	preferred indications are
	somatostatin or	complications associated with
	glucocorticoids. ATTC# CRL-	insulin resistance.
	1777 Refs: Lord and	
	Ashcroft. Biochem. J. 219:	
	547-551; Santerre et al. Proc.	
	Natl. Acad. Sci. USA 78:	

			4339-4343, 1981.	
HFABG18	621	Activation of	Kinase assay. Kinase assays,	A highly preferred
		Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
		Signaling Pathway	assay, for ERK signal	includes a method for
			transduction that regulate cell	stimulating adipocyte
			proliferation or differentiation	proliferation. An alternative
			are well known in the art and	highly preferred embodiment
			may be used or routinely	of the invention includes a
			modified to assess the ability	method for inhibiting
			of polypeptides of the	adipocyte proliferation. A
			invention (including antibodies	highly preferred embodiment
			and agonists or antagonists of	of the invention includes a
			the invention) to promote or	method for stimulating
			inhibit cell proliferation,	adipocyte differentiation. An
			activation, and differentiation.	alternative highly preferred
			Exemplary assays for ERK	embodiment of the invention
			kinase activity that may be	includes a method for
			used or routinely modified to	inhibiting adipocyte
			test ERK kinase-induced	differentiation. A highly
			activity of polypeptides of the	preferred embodiment of the
			invention (including antibodies	invention includes a method
			and agonists or antagonists of	for stimulating (e.g.,
			the invention) include the	increasing) adipocyte
			assays disclosed in Forrer et	activation. An alternative
			al., Biol Chem 379(8-9):1101-	highly preferred embodiment
			1110 (1998); Le Marchand-	of the invention includes a
			Brustel Y, Exp Clin	method for inhibiting the
			Endocrinol Diabetes	activation of (e.g., decreasing)
			107(2):126-132 (1999);	and/or inactivating adipocytes.
			Kyriakis JM, Biochem Soc	Highly preferred indications
			Symp 64:29-48 (1999); Chang	include endocrine disorders

	and Karin, Nature	(e.g., as described below under
•	410(6824):37-40 (2001); and	"Endocrine Disorders").
	Cobb MH, Prog Biophys Mol	Highly preferred indications
	Biol 71(3-4):479-500 (1999);	also include neoplastic
-	the contents of each of which	diseases (e.g., lipomas,
	are herein incorporated by	liposarcomas, and/or as
	reference in its entirety.	described below under
	Mouse adipocyte cells that	"Hyperproliferative
	may be used according to these	Disorders"). Preferred
	assays are publicly available	indications include blood
	(e.g., through the ATCC).	disorders (e.g., hypertension,
	Exemplary mouse adipocyte	congestive heart failure, blood
	cells that may be used	vessel blockage, heart disease,
	 according to these assays	stroke, impotence and/or as
	 include 3T3-L1 cells. 3T3-L1	described below under
	 is an adherent mouse	"Immune Activity",
	 preadipocyte cell line that is a	"Cardiovascular Disorders",
	 continuous substrain of 3T3	and/or "Blood-Related
	fibroblast cells developed	Disorders"), immune disorders
	 through clonal isolation and	(e.g., as described below under
	 undergo a pre-adipocyte to	"Immune Activity"), neural
	 adipose-like conversion under	disorders (e.g., as described
	appropriate differentiation	below under "Neural Activity
	conditions known in the art.	and Neurological Diseases"),
		and infection (e.g., as
		described below under
		"Infectious Disease").
		A highly preferred indication
		is diabetes mellitus. An
		additional highly preferred
-		indication is a complication

associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment
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									-	-																				

	(e.g., diahetic retinonathy and
	blindness), ulcers and impaired
	 wound healing, infection (e.g.,
	infectious diseases and
-	disorders as described in the
	"Infectious Diseases" section
	below (particularly of the
	 urinary tract and skin). An
	additional highly preferred
	indication is obesity and/or
	complications associated with
	obesity. Additional highly
	preferred indications include
	weight loss or alternatively,
	weight gain. Additional
	 highly preferred indications are
	 complications associated with
	insulin resistance.
	 Additional highly preferred
	indications are disorders of the
	musculoskeletal systems
	including myopathies,
	muscular dystrophy, and/or as
	described herein.
	Additional highly preferred
	indications include,
	 hypertension, coronary artery
	 disease, dyslipidemia,
	gallstones, osteoarthritis,
	degenerative arthritis, eating
	disorders, fibrosis, cachexia,

				and kidney diseases or
				disorders. Preferred
				indications include neoplasms
				and cancer, such as,
				lymphoma, leukemia and
				breast, colon, and kidney
				cancer. Additional preferred
				indications include melanoma,
				prostate, lung, pancreatic,
				esophageal, stomach, brain,
				liver, and urinary cancer.
	-			Highly preferred indications
	•			include lipomas and
	-			liposarcomas. Other preferred
				indications include benign
				dysproliferative disorders and
				pre-neoplastic conditions, such
				as, for example, hyperplasia,
				metaplasia, and/or dysplasia.
HFABG18	621	Protection from	Caspase Apoptosis Rescue.	A highly preferred
		Endothelial Cell	Assays for caspase apoptosis	embodiment of the invention
		Apoptosis.	rescue are well known in the	includes a method for
			art and may be used or	stimulating endothelial cell
			routinely modified to assess	growth. An alternative highly
			the ability of the polypeptides	preferred embodiment of the
			of the invention (including	invention includes a method
			antibodies and agonists or	for inhibiting endothelial cell
			antagonists of the invention) to	growth. A highly preferred
			inhibit caspase protease-	embodiment of the invention
			mediated apoptosis.	includes a method for
			Exemplary assays for caspase	stimulating endothelial cell

	apoptosis that may be used or	nroliferation An alternative
	routinely modified to test	highly preferred embodiment
	caspase apoptosis rescue of	of the invention includes a
	polypeptides of the invention	method for inhibiting
	(including antibodies and	endothelial cell proliferation.
	agonists or antagonists of the	A highly preferred
	invention) include the assays	embodiment of the invention
	disclosed in Romeo et al.,	includes a method for
	Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
	(2000); Messmer et al., Br J	growth. An alternative highly
	Pharmacol 127(7): 1633-1640	preferred embodiment of the
	(1999); and J Atheroscler	invention includes a method
	Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
	the contents of each of which	growth. A highly preferred
	are herein incorporated by	embodiment of the invention
	reference in its entirety.	includes a method for
	Endothelial cells that may be	stimulating apoptosis of
	used according to these assays	endothelial cells. An
-	are publicly available (e.g.,	alternative highly preferred
	through commercial sources).	embodiment of the invention
	Exemplary endothelial cells	includes a method for
	that may be used according to	inhibiting (e.g., decreasing)
	these assays include bovine	apoptosis of endothelial cells.
	aortic endothelial cells	A highly preferred
	(bAEC), which are an example	embodiment of the invention
-	of endothelial cells which line	includes a method for
	blood vessels and are involved	stimulating angiogenisis. An
	in functions that include, but	alternative highly preferred
	are not limited to,	embodiment of the invention
-	angiogenesis, vascular	includes a method for
	permeability, vascular tone,	inhibiting angiogenesis. A

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highly preferred embodiment of the invention includes a method for reducing cardiac	hypertrophy. An alternative highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neopiastic diseases (e.g., as	described below under	hyperpromeranve Disorders,) and disorders of	the cardiovascular system	me caldiovasculal system	(e.g., heart disease, congestive	mean railine, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic
and immune cell extravasation.		-																						-			
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disorders (e.g., systemic	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also
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include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud's	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from
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balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring,	ischemia reperfusion injury, rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include
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				autoimmune diseases (e.g.,
				rheumatoid arthritis, systemic
				lupus erythematosis, multiple
				sclerosis and/or as described
				below) and
				immunodeficiencies (e.g., as
				described below). Additional
				preferred indications include
				inflammation and
				inflammatory disorders (such
				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
				and Crohn's disease), and pain
				management.
 HFABG18	621	Production of	IFNgamma FMAT. IFNg plays	A highly preferred
		IFNgamma using a	a central role in the immune	embodiment of the invention
		T cells	system and is considered to be	includes a method for
			a proinflammatory cytokine.	stimulating the production of
	_		IFNg promotes TH1 and	IFNg. An alternative highly
			inhibits TH2 differentiation;	preferred embodiment of the
			promotes IgG2a and inhibits	invention includes a method
			IgE secretion; induces	for inhibiting the production of
			macrophage activation; and	IFNg. Highly preferred
			increases MHC expression.	indications include blood
			Assays for immunomodulatory	disorders (e.g., as described
			proteins produced by T cells	below under "Immune
			and NK cells that regulate a	Activity", "Blood-Related
			variety of inflammatory	Disorders", and/or
			activities and inhibit TH2	"Cardiovascular Disorders"),
			helper cell functions are well	and infection (e.g., viral

infections, tuberculosis,	intections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"), Highly preferred
known in the art and may be	asca of founding Illouined to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160
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	(2000); Gonzalez et al., J Clin	indications include neoplasms
	Lab Anal 8(5):225-233 (1995);	
	Billiau et al., Ann NY Acad	
	Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
	et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
-	15:749-795 (1997), and	esophageal, stomach, brain,
	Rheumatology (Oxford)	liver and urinary cancer. Other
	38(3):214-20 (1999), the	preferred indications include
	contents of each of which are	benign dysproliferative
	herein incorporated by	disorders and pre-neoplastic
	reference in its entirety.	conditions, such as, for
	Human T cells that may be	example, hyperplasia,
	used according to these assays	metaplasia, and/or dysplasia.
	may be isolated using	Preferred indications include
	techniques disclosed herein or	anemia, pancytopenia,
	otherwise known in the art.	leukopenia, thrombocytopenia,
	Human T cells are primary	Hodgkin's disease, acute
	human lymphocytes that	lymphocytic anemia (ALL),
	mature in the thymus and	plasmacytomas, multiple
	express a T Cell receptor and	myeloma, Burkitt's lymphoma,
	CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
-	cells mediate humoral or cell-	disease, inflammatory bowel
	mediated immunity and may	disease, sepsis, neutropenia,
	be preactivated to enhance	neutrophilia, psoriasis,
	responsiveness to	suppression of immune
	immunomodulatory factors.	reactions to transplanted
		organs and tissues,
		hemophilia, hypercoagulation,
		diabetes mellitus, endocarditis,
		meningitis, Lyme Disease,
		asthma and allergy.

HFABH95	622	Stimulation of	Assays for measuring secretion	A highly preferred
		insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
		from pancreatic	the art and may be used or	An additional highly preferred
		beta cells.	routinely modified to assess	indication is a complication
			the ability of polypeptides of	associated with diabetes (e.g.,
			the invention (including	diabetic retinopathy, diabetic
			antibodies and agonists or	nephropathy, kidney disease
			antagonists of the invention) to	(e.g., renal failure,
			stimulate insulin secretion.	nephropathy and/or other
			For example, insulin secretion	diseases and disorders as
			is measured by FMAT using	described in the "Renal
			anti-rat insulin antibodies.	Disorders" section below),
			Insulin secretion from	diabetic neuropathy, nerve
			pancreatic beta cells is	disease and nerve damage
			upregulated by glucose and	(e.g., due to diabetic
			also by certain	neuropathy), blood vessel
			proteins/peptides, and	blockage, heart disease, stroke,
			disregulation is a key	impotence (e.g., due to diabetic
			component in diabetes.	neuropathy or blood vessel
			Exemplary assays that may be	blockage), seizures, mental
			used or routinely modified to	confusion, drowsiness,
			test for stimulation of insulin	nonketotic hyperglycemic-
			secretion (from pancreatic	hyperosmolar coma,
		-	cells) by polypeptides of the	cardiovascular disease (e.g.,
			invention (including antibodies	heart disease, atherosclerosis,
			and agonists or antagonists of	microvascular disease,
			the invention) include assays	hypertension, stroke, and other
			disclosed in: Ahren, B., et al.,	diseases and disorders as
			Am J Physiol, 277(4 Pt	described in the
			2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
			al., Endocrinology,	section below), dyslipidemia,

				138(9):3735-40 (1997): Kim.	endocrine disorders (as
				K.H. et al FFBS Lett	described in the "Endocrino
				377(2):237-9 (1995); and.	Disorders" section helow)
	-			Miraglia S et. al., Journal of	neuropathy, vision impairment
				Biomolecular Screening,	(e.g., diabetic retinopathy and
				4:193-204 (1999), the contents	blindness), ulcers and impaired
				of each of which is herein	wound healing, and infection
			•	incorporated by reference in its	(e.g., infectious diseases and
				entirety. Pancreatic cells that	disorders as described in the
				may be used according to these	"Infectious Diseases" section
	_			assays are publicly available	below, especially of the
				(e.g., through the ATCC)	urinary tract and skin), carpal
			_	and/or may be routinely	tunnel syndrome and
_				generated. Exemplary	Dupuytren's contracture).
				pancreatic cells that may be	An additional highly preferred
		-		used according to these assays	indication is obesity and/or
				include rat INS-1 cells. INS-1	complications associated with
		-		cells are a semi-adherent cell	obesity. Additional highly
				line established from cells	preferred indications include
-				isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
				These cells retain	highly preferred indications are
				characteristics typical of native	complications associated with
				pancreatic beta cells including	insulin resistance.
		-		glucose inducible insulin	
_				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:167.	
	HFAEF57	623	Regulation of	Assays for the regulation of	A highly preferred
			transcription	transcription through the FAS	indication is diabetes mellitus.
			through the FAS	promoter element are well-	An additional highly preferred

	promoter element	known in the art and may be	indication is a complication
	in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
		assess the ability of	diabetic retinopathy, diabetic
		polypeptides of the invention	nephropathy, kidney disease
		(including antibodies and	(e.g., renal failure,
-		agonists or antagonists of the	nephropathy and/or other
		invention) to activate the FAS	diseases and disorders as
		promoter element in a reporter	described in the "Renal
		construct and to regulate	Disorders" section below),
		transcription of FAS, a key	diabetic neuropathy, nerve
		enzyme for lipogenesis. FAS	disease and nerve damage
		promoter is regulated by many	(e.g., due to diabetic
		transcription factors including	neuropathy), blood vessel
		SREBP. Insulin increases FAS	blockage, heart disease, stroke,
		gene transcription in livers of	impotence (e.g., due to diabetic
		diabetic mice. This	neuropathy or blood vessel
		stimulation of transcription is	blockage), seizures, mental
		also somewhat glucose	confusion, drowsiness,
		dependent. Exemplary assays	nonketotic hyperglycemic-
		that may be used or routinely	hyperosmolar coma,
		modified to test for FAS	cardiovascular disease (e.g.,
		promoter element activity (in	heart disease, atherosclerosis,
		hepatocytes) by polypeptides	microvascular disease,
		of the invention (including	hypertension, stroke, and other
		antibodies and agonists or	diseases and disorders as
		antagonists of the invention)	described in the
		include assays disclosed in	"Cardiovascular Disorders"
		Xiong, S., et al., Proc Natl	section below), dyslipidemia,
		Acad Sci U.S.A., 97(8):3948-	endocrine disorders (as
		53 (2000); Roder, K., et al.,	described in the "Endocrine
		Eur J Biochem, 260(3):743-51	Disorders" section below),

				(1999); Oskouian B, et al.,	neuropathy, vision impairment
				Biochem J, 317 (Pt 1):257-65	(e.g., diabetic retinopathy and
_				(1996); Berger, et al., Gene	blindness), ulcers and impaired
				66:1-10 (1988); and, Cullen,	wound healing, and infection
				B., et al., Methods in Enzymol.	(e.g., infectious diseases and
	_	_		216:362–368 (1992), the	disorders as described in the
				contents of each of which is	"Infectious Diseases" section
				herein incorporated by	below, especially of the
				reference in its entirety.	urinary tract and skin), carpal
				Hepatocytes that may be used	tunnel syndrome and
				according to these assays, such	Dupuytren's contracture).
			-	as H4IIE cells, are publicly	An additional highly preferred
				available (e.g., through the	indication is obesity and/or
				ATCC) and/or may be	complications associated with
				routinely generated.	obesity. Additional highly
	-			Exemplary hepatocytes that	preferred indications include
				may be used according to these	weight loss or alternatively,
	-			assays include rat liver	weight gain. Aditional
				hepatoma cell line(s) inducible	highly preferred indications are
				with glucocorticoids, insulin,	complications associated with
				or cAMP derivatives.	insulin resistance.
	HFAMH77	624	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred

regulate the serum response
factors and modulate the
expression of genes involved
in growth. Exemplary assays
for transcription through the
SRE that may be used or
routinely modified to test SRE
activity of the polypeptides of
the invention (including
antibodies and agonists or
antagonists of the invention)
include assays disclosed in
Berger et al., Gene 66:1-10
(1998); Cullen and Malm,
Methods in Enzymol 216:362-
368 (1992); Henthorn et al.,
Proc Natl Acad Sci USA
85:6342-6346 (1988); and
Black et al., Virus Genes
12(2):105-117 (1997), the
content of each of which are
herein incorporated by
reference in its entirety.
cells that may be used
according to these assays are
publicly available (e.g.,
through the ATCC).
Exemplary mouse T cells that
may be used according to these
assays include the CTLL cell
line, which is an IL-2

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highly preferred indications include neoplasms and cancers. such as, for example	leukemia, lymphoma,	melanoma, glioma (e.g.,	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,
dependent suspension culture of T cells with cytotoxic activity.							_																				
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diabetes mellitus, endocarditis,	meningitis, Lyme Disease, cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication	is infection (e.g., an infectious	disease as described below	624 Production of	ama using a a central role in the immune eml	T cells system and is considered to be includes a method for	a proinflammatory cytokine. stimulating the production of	inhibits TH2 differentiation; preferred embodiment of the	promotes IgG2a and inhibits invention includes a method	 	indications	Assays for immunomodulatory disorders (e.g., as described	 and NK cells that regulate a Activity", "Blood-Related	variety of inflammatory Disorders", and/or	 	known in the art and may be infections, tuberculosis,	diffied to	assess the ability of chronic granulomatosus	polypeptides of the invention disease and malignant	(including antibodies and osteoporosis, and/or as	agonists or antagonists of the
		_				HFAMH77	_								 _		 						

	immunomodulation, regulate	preferred indications include
	inflammatory activities,	autoimmune disease (e.g.,
	modulate TH2 helper cell	rheumatoid arthritis, systemic
	function, and/or mediate	lupus erythematosis, multiple
	humoral or cell-mediated	sclerosis and/or as described
	immunity. Exemplary assays	below), immunodeficiency
	that test for	(e.g., as described below),
	immunomodulatory proteins	boosting a T cell-mediated
	evaluate the production of	immune response, and
	cytokines, such as Interferon	suppressing a T cell-mediated
	gamma (IFNg), and the	immune response. Additional
	activation of T cells. Such	highly preferred indications
	assays that may be used or	include inflammation and
	routinely modified to test	inflammatory disorders.
-	immunomodulatory activity of	Additional preferred
	polypeptides of the invention	indications include idiopathic
	(including antibodies and	pulmonary fibrosis. Highly
	agonists or antagonists of the	preferred indications include
	invention) include the assays	neoplastic diseases (e.g.,
	disclosed in Miraglia et al., J	leukemia, lymphoma,
	Biomolecular Screening 4:193-	melanoma, and/or as described
	204 (1999); Rowland et al.,	below under
	"Lymphocytes: a practical	"Hyperproliferative
	approach" Chapter 6:138-160	Disorders"). Highly preferred
	(2000); Gonzalez et al., J Clin	indications include neoplasms
	Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
	Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
	Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
	et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
	15:749-795 (1997), and	esophageal, stomach, brain,
	Rheumatology (Oxford)	liver and urinary cancer. Other

				38(3):214-20 (1999), the	preferred indications include
				contents of each of which are	benign dysproliferative
				herein incorporated by	disorders and pre-neoplastic
				reference in its entirety.	conditions, such as, for
				Human T cells that may be	example, hyperplasia,
				used according to these assays	metaplasia, and/or dysplasia.
				may be isolated using	Preferred indications include
				techniques disclosed herein or	anemia, pancytopenia,
				otherwise known in the art.	leukopenia, thrombocytopenia,
				Human T cells are primary	Hodgkin's disease, acute
				human lymphocytes that	lymphocytic anemia (ALL),
				mature in the thymus and	plasmacytomas, multiple
				express a T Cell receptor and	myeloma, Burkitt's lymphoma,
				CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
				cells mediate humoral or cell-	disease, inflammatory bowel
				mediated immunity and may	disease, sepsis, neutropenia,
				be preactivated to enhance	neutrophilia, psoriasis,
				responsiveness to	suppression of immune
_	~			immunomodulatory factors.	reactions to transplanted
_					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
HFAMH77	177	624	Droduotion of	DANTES ENTAT A	asthma and allergy.
		-	Todactor of	MAINTES FIMAL. ASSAYS IOF	
			RANTES in	immunomodulatory proteins	
_			endothelial cells	that induce chemotaxis of T	
			(such as human	cells, monocytes, and	
			umbilical vein	eosinophils are well known in	
			endothelial cells	the art and may be used or	
			(HUVEC))	routinely modified to assess	

the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	induce chemotaxis, and/or	mediate humoral or cell-	mediated immunity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as RANTES,	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407
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	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include blood disorders (e.g.,
which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of
	Production of TNF alpha by dendritic cells
	625
	HFCCQ50

	the invention (including	as described below under
	antibodies and agonists or	"Immune Activity", "Blood-
	antagonists of the invention) to	Related Disorders", and/or
	mediate immunomodulation,	"Cardiovascular Disorders"),
	modulate inflammation and	Highly preferred indications
	cytotoxicity. Exemplary	include autoimmune diseases
-	assays that test for	(e.g., rheumatoid arthritis,
	immunomodulatory proteins	systemic lupus erythematosis,
	evaluate the production of	Crohn"s disease, multiple
	cytokines such as tumor	sclerosis and/or as described
	necrosis factor alpha (TNFa),	below), immunodeficiencies
	and the induction or inhibition	(e.g., as described below),
	of an inflammatory or	boosting a T cell-mediated
	eytotoxic response. Such	immune response, and
	assays that may be used or	suppressing a T cell-mediated
	routinely modified to test	immune response. Additional
	immunomodulatory activity of	highly preferred indications
	polypeptides of the invention	include inflammation and
	(including antibodies and	inflammatory disorders, and
	agonists or antagonists of the	treating joint damage in
	invention) include assays	patients with rheumatoid
	disclosed in Miraglia et al., J	arthritis. An additional highly
	Biomolecular Screening 4:193-	preferred indication is sepsis.
	204(1999); Rowland et al.,	Highly preferred indications
	"Lymphocytes: a practical	include neoplastic diseases
	approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
	(2000); Verhasselt et al., Eur J	and/or as described below
	Immunol 28(11):3886-3890	under "Hyperproliferative
	(1198); Dahlen et al., J	Disorders"). Additionally,
-	Immunol 160(7):3585-3593	highly preferred indications
	(1998); Verhasselt et al., J	include neoplasms and

	preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia,	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion iniury, and
Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety.	Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen	and/or cytokines, initiate and upregulate T cell proliferation and functional activities.

					asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
H	HFCCQ50	625	Production of IL-4	IL-4 FMAT. Assays for	A highly preferred
				immunomodulatory proteins	embodiment of the invention
				secreted by TH2 cells that	includes a method for
				stimulate B cells, T cells,	stimulating (e.g., increasing)
				macrophages and mast cells	IL-4 production. An alternative
				and promote polarization of	highly preferred embodiment
				CD4+ cells into TH2 cells are	of the invention includes a
				well known in the art and may	method for inhibiting (e.g.,
				be used or routinely modified	reducing) IL-4 production.
				to assess the ability of	A highly preferred indication
				polypeptides of the invention	includes asthma. A highly
				(including antibodies and	preferred indication includes
				agonists or antagonists of the	allergy. A highly preferred
				invention) to mediate	indication includes rhinitis.
				immunomodulation, stimulate	Additional highly preferred
				immune cells, modulate	indications include
				immune cell polarization,	inflammation and
				and/or mediate humoral or	inflammatory disorders.
			-	cell-mediated immunity.	Highly preferred indications
				Exemplary assays that test for	include neoplastic diseases
				immunomodulatory proteins	(e.g., leukemia, lymphoma,
				evaluate the production of	melanoma, and/or as described
				cytokines, such as IL-4, and	below under
-				the stimulation of immune	"Hyperproliferative
				cells, such as B cells, T cells,	Disorders"). Preferred
				macrophages and mast cells.	indications include neoplasms

			express a T cell receptor and CD3, CD4, or CD8. These	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
			cells mediate humoral or cell-	arthritis, AIDS, granulomatous
-	-		be preactivated to enhance	disease, initialinitiatory bowel
 			responsiveness to	neutrophilia, psoriasis,
 <u>.</u>			immunomodulatory factors.	suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
	-			diabetes mellitus, endocarditis,
				meningitis, and Lyme Disease.
				An additonal preferred
				indication is infection (e.g., an
				infectious disease as described
				below under "Infectious
				Disease").
HFCCQ50	625	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include inflammation and
		through NFKB	NFKB response element are	inflammatory disorders.
		response element in	well-known in the art and may	Highly preferred indications
		immune cells (such	be used or routinely modified	include immunological and
		as the Jurkat human	to assess the ability of	hematopoietic disorders (e.g.,
		T cell line).	polypeptides of the invention	as described below under
			(including antibodies and	"Immune Activity", "Blood-
	-		agonists or antagonists of the	Related Disorders", and/or
			invention) to regulate NFKB	"Cardiovascular Disorders").
			transcription factors and	Highly preferred indications
			modulate expression of	include autoimmune diseases
			immunomodulatory genes.	(e.g., rheumatoid arthritis,
			Exemplary assays for	systemic lupus erythematosis,

	transcription through the	multiple sclerosis and/or as
	NFKB response element that	described below), and
	may be used or rountinely	immunodeficiencies (e.g., as
	modified to test NFKB-	described below). An
	response element activity of	additional highly preferred
	polypeptides of the invention	indication is infection (e.g.,
	(including antibodies and	AIDS, and/or an infectious
	agonists or antagonists of the	disease as described below
	invention) include assays	under "Infectious Disease").
	disclosed in Berger et al., Gene	Highly preferred indications
	66:1-10 (1998); Cullen and	include neoplastic diseases
	Malm, Methods in Enzymol	(e.g., melanoma, leukemia,
	216:362-368 (1992); Henthorn	lymphoma, and/or as described
	et al., Proc Natl Acad Sci USA	below under
	85:6342-6346 (1988); Valle	"Hyperproliferative
	Blazquez et al, Immunology	Disorders"). Highly preferred
	90(3):455-460 (1997);	indications include neoplasms
	Aramburau et al., J Exp Med	and cancers, such
	82(3):801-810 (1995); and	as,melanoma, renal cell
	Fraser et al., 29(3):838-844	carcinoma, leukemia,
	(1999), the contents of each of	lymphoma, and prostate,
	which are herein incorporated	breast, lung, colon, pancreatic,
	by reference in its entirety. T	esophageal, stomach, brain,
	cells that may be used	liver and urinary cancer. Other
	according to these assays are	preferred indications include
	publicly available (e.g.,	benign dysproliferative
	through the ATCC). T cells	disorders and pre-neoplastic
	that may be used according to	conditions, such as, for
-	these assays are publicly	example, hyperplasia,
	available (e.g., through the	metaplasia, and/or dysplasia.
	ATCC). Exemplary human T	Preferred indications also

include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Infection, Cancer, Hypersensitivity, and Atherosclerosis.
cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of
	Activation of transcription through GAS response element in immune cells (such as monocytes).
	625
	HFCCQ50

cell functions. Exemplary	assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Gustafson KS, et	al., J Biol Chem,	271(33):20035-20046 (1996);	Eilers A, et al.,	Immunobiology, 193(2-4):328-	333 (1995); Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary immune cells that	may be used according to these	assays are publicly available
																	-						-							
				-																							_			

			(e.g., through the ATCC). Exemplary immune cells that may be used according to these assays include the U937 cell line, which is a monocytic cell line.	
 HFCEB3/	070	Kegulation of transcription of Malic Enzyme in adipocytes	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis.	A fightly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below),
			n is	diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis,

invention as and ists of the ists of the issays er, R.S., et y. 98); et al., Mol 361-9 et al., J 17 (1997); 66:1-10 66:1-10 hy by every. In the which is by by every. In the which is by and by every. In the which is every.	(in adipoocytes) by	microvascular disease.
	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	 disclosed in: Streeper, R.S., et	section below), dyslipidemia,
	al., Mol Endocrinol,	endocrine disorders (as
	12(11):1778-91 (1998);	described in the "Endocrine
	Garcia-Jimenez, C., et al., Mol	Disorders" section below),
	 Endocrinol, 8(10):1361-9	neuropathy, vision impairment
	 (1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
	Biol Chem, 274(25):17997-	blindness), ulcers and impaired
	8004 (1999); Ijpenberg, A., et	wound healing, and infection
	al., J Biol Chem,	(e.g., infectious diseases and
	272(32):20108-20117 (1997);	disorders as described in the
	Berger, et al., Gene 66:1-10	"Infectious Diseases" section
	(1988); and, Cullen, B., et al.,	below, especially of the
	Methods in Enzymol.	urinary tract and skin), carpal
	216:362–368 (1992), the	tunnel syndrome and
	 contents of each of which is	Dupuytren's contracture).
	herein incorporated by	An additional highly preferred
	reference in its entirety.	indication is obesity and/or
	Hepatocytes that may be used	complications associated with
	according to these assays are	obesity. Additional highly
	publicly available (e.g.,	preferred indications include
	through the ATCC) and/or	weight loss or alternatively,
	may be routinely generated.	weight gain. Aditional
	Exemplary hepatocytes that	highly preferred indications are
	 may be used according to these	complications associated with
liver hepatoma cell line.	assays includes the H4IIE rat	insulin resistance.
	liver hepatoma cell line.	

	HFFAD59	627	Regulation of	Assays for the regulation of	A highly preferred indication
			transcription via	transcription through the	is diabetes mellins
			DMEF1 response	DMEF1 response element are	Additional highly preferred
			element in	well-known in the art and may	indications include
			adipocytes and pre-	be used or routinely modified	complications associated with
			adipocytes	to assess the ability of	diabetes (e.g., diabetic
				polypeptides of the invention	retinopathy, diabetic
				(including antibodies and	nephropathy, kidney disease
				agonists or antagonists of the	(e.g., renal failure,
				invention) to activate the	nephropathy and/or other
				DMEF1 response element in a	diseases and disorders as
				reporter construct (such as that	described in the "Renal
				containing the GLUT4	Disorders" section below),
				promoter) and to regulate	diabetic neuropathy, nerve
				insulin production. The	disease and nerve damage
				DMEF1 response element is	(e.g., due to diabetic
-				present in the GLUT4	neuropathy), blood vessel
				promoter and binds to MEF2	blockage, heart disease, stroke,
				transcription factor and another	impotence (e.g., due to diabetic
				transcription factor that is	neuropathy or blood vessel
				required for insulin regulation	blockage), seizures, mental
				of Glut4 expression in skeletal	confusion, drowsiness,
				muscle. GLUT4 is the primary	nonketotic hyperglycemic-
				insulin-responsive glucose	hyperosmolar coma,
				transporter in fat and muscle	cardiovascular disease (e.g.,
				tissue. Exemplary assays that	heart disease, atherosclerosis,
				may be used or routinely	microvascular disease,
				modified to test for DMEF1	hypertension, stroke, and other
				response element activity (in	diseases and disorders as
				adipocytes and pre-adipocytes)	described in the
				by polypeptides of the	"Cardiovascular Disorders"

invention (including antibodies	section below), dyslipidemia,
and agonists or antagonists of	endocrine disorders (as
the invention) include assays	described in the "Endocrine
disclosed in Thai, M.V., et al., J	Disorders" section below),
Biol Chem, 273(23):14285-92	neuropathy, vision impairment
(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
Chem, 275(21):16323-8	blindness), ulcers and impaired
(2000); Liu, M.L., et al., J Biol	wound healing, and infection
Chem, 269(45):28514-21	(e.g., infectious diseases and
(1994); "Identification of a 30-	disorders as described in the
base pair regulatory element	"Infectious Diseases" section
and novel DNA binding	below, especially of the
 protein that regulates the	urinary tract and skin). An
 human GLUT4 promoter in	additional highly preferred
 transgenic mice", J Biol Chem.	indication is obesity and/or
 2000 Aug 4;275(31):23666-73;	complications associated with
Berger, et al., Gene 66:1-10	obesity. Additional highly
(1988); and, Cullen, B., et al.,	preferred indications include
Methods in Enzymol.	weight loss or alternatively,
 216:362–368 (1992), the	weight gain. Additional highly
contents of each of which is	preferred indications are
herein incorporated by	complications associated with
reference in its entirety.	insulin resistance.
Adipocytes and pre-adipocytes	
that may be used according to	
these assays are publicly	
available (e.g., through the	
ATCC) and/or may be	
routinely generated.	
 Exemplary cells that may be	
used according to these assays	

	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Diseases"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as
include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays
	Activation of transcription through AP1 response element in immune cells (such as T-cells).
	627
	HFFAD59

	disclosed in Berger et al Gene	described below) Additional
	66:1-10 (1988); Cullen and	highly preferred indications
	Malm, Methods in Enzymol	include inflammation and
	216:362-368 (1992); Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	272(49):30806-30811 (1997);	lymphoma, and/or as described
	 Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	contents of each of which are	and cancers, such as, leukemia,
	 herein incorporated by	lymphoma, prostate, breast,
	reference in its entirety. T	lung, colon, pancreatic,
	cells that may be used	esophageal, stomach, brain,
	according to these assays are	liver, and urinary cancer. Other
	publicly available (e.g.,	preferred indications include
	 through the ATCC).	benign dysproliferative
	Exemplary mouse T cells that	disorders and pre-neoplastic
	may be used according to these	conditions, such as, for
	assays include the CTLL cell	example, hyperplasia,
	line, which is an IL-2	metaplasia, and/or dysplasia.
	 dependent suspension-culture	Preferred indications include
	cell line with cytotoxic	arthritis, asthma, AIDS,
	activity.	allergy, anemia, pancytopenia,
-		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,

					granulomatous disease, inflammatory bowel disease, sensis psoriasis sumpression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HFFAD59	627	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
-				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described
,-				Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),

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ediated	puı	l-mediate	Additio	lications	on and	ders, and	e in	atoid	onal high	is sepsi	dications	liseases	phoma,	below	erative	onally,	lications	pun	exampl	a,	e.g.,	solid	e, breast,	ıtic,	h, brain,	ncer. Oth	s include	ive	soplastic	
T cell-m	sponse, a	g a T cel	sponse.	erred inc	lammatic	ry disor	nt damag	th rheum	n additio	ndication	ferred in	plastic c	mia, lym	escribed	erprolife	. Additi	erred ind	plasms	ch as, for	ymphom	glioma (glioma),	l prostate	, pancrea	, stomacl	inary ca	dication	orolifera	nd pre-ne	•
boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	
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01 216:30	m et al.,	USA	8); and	Jenes	7), the	vhich are	by	ety. T	eq	ssays ar	.g.,		cells th	ing to th	TLL ce	.5	on cultur	oxic												
Enzyme	Hentho	cad Sci	46 (198	, Virus (17 (199	ach of v	porated	its entir	ay be us	these a	ailable (6	ATCC)	mouse T	d accord	de the C	is an IL-	uspensi	ith cytot												
Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC)	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.											
Me	368	Pro	85:0	Bla	12(con	her	refe	cell	acc	qnd	thrc	Exe	may	asse	line	deb	l Jo	acti											
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			example, hyperplasia,
			metaplasia, and/or dysplasia.
			Preferred indications include
			anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
			disease, inflammatory bowel
7.			disease, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted
			organs and tissues,
			hemophilia, hypercoagulation,
		•	diabetes mellitus, endocarditis,
			meningitis, Lyme Disease,
			cardiac reperfusion injury, and
			asthma and allergy. An
			additional preferred indication
			is infection (e.g., an infectious
			disease as described below
			under "Infectious Disease").
628	Activation of	Assays for the activation of	Preferred indications
	transcription	transcription through the AP1	include neoplastic diseases
	through AP1	response element are known in	(e.g., as described below under
	response element in	the art and may be used or	"Hyperproliferative
	immune cells (such	routinely modified to assess	Disorders"), blood disorders
	as T-cells).	the ability of polypeptides of	(e.g., as described below under

	the invention (including	"Immune Activity",
	antibodies and agonists or	"Cardiovascular Disorders",
	antagonists of the invention) to	and/or "Blood-Related
	modulate growth and other cell	Disorders"), and infection
	functions. Exemplary assays	(e.g., an infectious disease as
	for transcription through the	described below under
	AP1 response element that	"Infectious Disease"). Highly
	may be used or routinely	preferred indications include
	modified to test AP1-response	autoimmune diseases (e.g.,
	element activity of	rheumatoid arthritis, systemic
	polypeptides of the invention	lupus erythematosis, multiple
	(including antibodies and	sclerosis and/or as described
	agonists or antagonists of the	below) and
	invention) include assays	immunodeficiencies (e.g., as
	disclosed in Berger et al., Gene	described below). Additional
	66:1-10 (1988); Cullen and	highly preferred indications
	Malm, Methods in Enzymol	include inflammation and
-	216:362-368 (1992); Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	272(49):30806-30811 (1997);	lymphoma, and/or as described
	Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	contents of each of which are	and cancers, such as, leukemia,
	herein incorporated by	lymphoma, prostate, breast,
	reference in its entirety. T	lung, colon, pancreatic,
	cells that may be used	esophageal, stomach, brain,
	according to these assays are	liver, and urinary cancer. Other

				publicly available (e.g.,	preferred indications include
			_	through the ATCC).	benign dysproliferative
				Exemplary mouse T cells that	disorders and pre-neoplastic
				may be used according to these	conditions, such as, for
				assays include the CTLL cell	example, hyperplasia,
		-		line, which is an IL-2	metaplasia, and/or dysplasia.
				dependent suspension-culture	Preferred indications include
				cell line with cytotoxic	arthritis, asthma, AIDS,
				activity.	allergy, anemia, pancytopenia,
		-			leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
		-			myeloma, Burkitt's lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
	7011111				meningitis, and Lyme Disease.
<u> </u>	HFFAL30	879	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred

blood	escribed	ıne	Related		sorders"),	dications	e diseases	thritis,	hematosis,	ultiple	described	Ticiencies	elow),	ediated	pur	l-mediated	Additional	lications	on and	ders, and	ge in	natoid	onal highly	ı is sepsis.	dications	liseases	nphoma,	below	erative	;
indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn's disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	
ind	disc	pel	Act	Dis	<u>ڀ</u>			(e.g	sys	<u>2</u>	scle	pel	(e.g		<u>.m.</u>	dns	- Imr	hig	inc	linfl	trea	pati	art	pre	Hig	inc			m	-
regulate the serum response	factors and modulate the	expression of genes involved	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	

highly preferred indications include neoplasms and cancers, such as, for example,	leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic,	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL),	plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel	neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation,
dependent suspension culture of T cells with cytotoxic activity.						

	216:362-368 (1992); Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
-	272(49):30806-30811 (1997);	lymphoma, and/or as described
	Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	contents of each of which are	and cancers, such as, leukemia,
	herein incorporated by	lymphoma, prostate, breast,
-	reference in its entirety.	lung, colon, pancreatic,
	Mouse T cells that may be	esophageal, stomach, brain,
	used according to these assays	liver, and urinary cancer. Other
	are publicly available (e.g.,	preferred indications include
	through the ATCC).	benign dysproliferative
	Exemplary mouse T cells that	disorders and pre-neoplastic
	may be used according to these	conditions, such as, for
_	assays include the HT2 cell	example, hyperplasia,
	line, which is an IL-2	metaplasia, and/or dysplasia.
	dependent suspension culture	Preferred indications include
	cell line that also responds to	arthritis, asthma, AIDS,
	IL-4.	allergy, anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
-		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		granulomatous disease,
		inflammatory bowel disease,
		sepsis, psoriasis, suppression

					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
<u> </u>	HFGAD82	629	Stimulation of	Assays for measuring secretion	A highly preferred
			insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
			from pancreatic	the art and may be used or	An additional highly preferred
			beta cells.	routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
-				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
•				Insulin secretion from	diabetic neuropathy, nerve
-				pancreatic beta cells is	disease and nerve damage
				upregulated by glucose and	(e.g., due to diabetic
				also by certain	neuropathy), blood vessel
				proteins/peptides, and	blockage, heart disease, stroke,
				disregulation is a key	impotence (e.g., due to diabetic
				component in diabetes.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
				test for stimulation of insulin	nonketotic hyperglycemic-
				secretion (from pancreatic	hyperosmolar coma,
				cells) by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,
				the invention) include assays	hypertension, stroke, and other

Josip	disclosed in: Ahren B et al	diseases and disorders as
	Db: 21 277/4 Dt	december and disorders as
Am	Am J Physiol, 21/(4 Pt	described in the
	2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
al., E	indocrinology,	section below), dyslipidemia,
138(9	138(9):3735-40 (1997); Kim,	endocrine disorders (as
K.H.,	K.H., et al., FEBS Lett,	described in the "Endocrine
377(2	377(2):237-9 (1995); and,	Disorders" section below),
Mira	Miraglia S et. al., Journal of	neuropathy, vision impairment
Biom	Biomolecular Screening,	(e.g., diabetic retinopathy and
4:193	4:193-204 (1999), the contents	blindness), ulcers and impaired
of ea	of each of which is herein	wound healing, and infection
incor	incorporated by reference in its	(e.g., infectious diseases and
entire	entirety. Pancreatic cells that	disorders as described in the
may	may be used according to these	"Infectious Diseases" section
assay	assays are publicly available	below, especially of the
(e.g.,	(e.g., through the ATCC)	urinary tract and skin), carpal
o/pue	and/or may be routinely	tunnel syndrome and
laued gener	generated. Exemplary	Dupuytren's contracture).
panci	pancreatic cells that may be	An additional highly preferred
pasn	used according to these assays	indication is obesity and/or
inclu	include rat INS-1 cells. INS-1	complications associated with
cells	cells are a semi-adherent cell	obesity. Additional highly
line e	line established from cells	preferred indications include
isolat	isolated from an X-ray induced	weight loss or alternatively,
rat tra	rat transplantable insulinoma.	weight gain. Aditional
These	These cells retain	highly preferred indications are
chara	characteristics typical of native	complications associated with
panci	pancreatic beta cells including	insulin resistance.
oonlg	glucose inducible insulin	
Secre	secretion. References: Asfari	
et al.	et al. Endocrinology 1992	

			130:167.	
HFIUR10	630	Regulation of	Assays for the regulation of	A highly preferred indication
		viability and	viability and proliferation of	is diabetes mellitus. An
		proliferation of	cells in vitro are well-known in	additional highly preferred
		pancreatic beta	the art and may be used or	indication is a complication
		cells.	routinely modified to assess	associated with diabetes (e.g.,
			the ability of polypeptides of	diabetic retinopathy, diabetic
			the invention (including	nephropathy, kidney disease
			antibodies and agonists or	(e.g., renal failure,
			antagonists of the invention) to	nephropathy and/or other
			regulate viability and	diseases and disorders as
			proliferation of pancreatic beta	described in the "Renal
			cells. For example, the Cell	Disorders" section below),
			Titer-Glo luminescent cell	diabetic neuropathy, nerve
			viability assay measures the	disease and nerve damage
			number of viable cells in	(e.g., due to diabetic
			culture based on quantitation	neuropathy), blood vessel
			of the ATP present which	blockage, heart disease, stroke,
			signals the presence of	impotence (e.g., due to diabetic
			metabolically active cells.	neuropathy or blood vessel
			Exemplary assays that may be	blockage), seizures, mental
			used or routinely modified to	confusion, drowsiness,
			test regulation of viability and	nonketotic hyperglycemic-
			proliferation of pancreatic beta	hyperosmolar coma,
			cells by polypeptides of the	cardiovascular disease (e.g.,
			invention (including antibodies	heart disease, atherosclerosis,
			and agonists or antagonists of	microvascular disease,
			the invention) include assays	hypertension, stroke, and other
			disclosed in: Ohtani KI, et al.,	diseases and disorders as
			Endocrinology, 139(1):172-8	described in the
			(1998); Krautheim A, et al,	"Cardiovascular Disorders"

			Exp Clin Endocrinol Diabetes,	section below), dyslipidemia,
			107 (1):29-34 (1999), the	endocrine disorders (as
			contents of each of which is	described in the "Endocrine
			herein incorporated by	Disorders" section below),
			reference in its entirety.	neuropathy, vision impairment
			Pancreatic cells that may be	(e.g., diabetic retinopathy and
			used according to these assays	blindness), ulcers and impaired
			are publicly available (e.g.,	wound healing, and infection
			through the ATCC) and/or	(e.g., infectious diseases and
			may be routinely generated.	disorders as described in the
			Exemplary pancreatic cells that	"Infectious Diseases" section
			may be used according to these	below, especially of the
			assays include HITT15 Cells.	urinary tract and skin), carpal
			HITT15 are an adherent	tunnel syndrome and
			epithelial cell line established	Dupuytren's contracture). An
			from Syrian hamster islet cells	additional highly preferred
			transformed with SV40. These	indication is obesity and/or
			cells express glucagon,	complications associated with
			somatostatin, and	obesity. Additional highly
			glucocorticoid receptors. The	preferred indications include
			cells secrete insulin, which is	weight loss or alternatively,
			stimulated by glucose and	weight gain. Additional highly
			glucagon and suppressed by	preferred indications are
			somatostatin or	complications associated with
			glucocorticoids. ATTC# CRL-	insulin resistance.
			1777 Refs: Lord and	
			Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc.	
			Natl. Acad. Sci. USA 78:	
			4339-4343, 1981.	
HFTBM50	631	Insulin Secretion	Assays for measuring secretion	A highly preferred indication

			<u>.</u>				
is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g.,	diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other	diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve	disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel	blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel	blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma,	cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other	diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as
of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of	the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion.	For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies.	pancreatic beta cells is upregulated by glucose and also by certain	proteins/peptides, and disregulation is a key component in diabetes.	Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic	cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in: Shimizu, H., et al., Endocr J, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al.,

Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
(1998); Olson, L.K., et al., J	Disorders" section below),
Biol Chem, 271(28):16544-52	neuropathy, vision impairment
(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
Journal of Biomolecular	blindness), ulcers and impaired
Screening, 4:193-204 (1999),	wound healing, and infection
the contents of each of which	(e.g., infectious diseases and
is herein incorporated by	disorders as described in the
 reference in its entirety.	"Infectious Diseases" section
Pancreatic cells that may be	below, especially of the
used according to these assays	urinary tract and skin), carpal
are publicly available (e.g.,	tunnel syndrome and
 through the ATCC) and/or	Dupuytren's contracture).
may be routinely generated.	An additional highly preferred
Exemplary pancreatic cells that	indication is obesity and/or
 may be used according to these	complications associated with
assays include HITT15 Cells.	obesity. Additional highly
HITT15 are an adherent	preferred indications include
epithelial cell line established	weight loss or alternatively,
from Syrian hamster islet cells	weight gain. Additional highly
transformed with SV40. These	preferred indications are
cells express glucagon,	complications associated with
somatostatin, and	insulin resistance.
glucocorticoid receptors. The	
cells secrete insulin, which is	
stimulated by glucose and	
glucagon and suppressed by	
 somatostatin or	
 glucocorticoids. ATTC# CRL-	
1777 Refs: Lord and	
Ashcroft. Biochem. J. 219:	

			547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	
HFTBM50	631	Production of IL-10	Assays for production of IL-10 and activation of T-cells are	Highly preferred indications include allergy and asthma.
		cells.	well known in the art and may	Additional highly preferred
			be used or routinely modified	indications include immune
			to assess the ability of	and hematopoietic disorders
			polypeptides of the invention	(e.g., as described below under
			(including antibodies and	"Immune Activity", and
			agonists or antagonists of the	"Blood-Related Disorders"),
 			invention) to stimulate or	autoimmune diseases (e.g.,
 			inhibit production of IL-10	rheumatoid arthritis, systemic
 			and/or activation of T-cells.	lupus erythematosis, Crohn"s
			Exemplary assays that may be	disease, multiple sclerosis
			used or routinely modified to	and/or as described below),
			assess the ability of	immunodeficiencies (e.g., as
	_		polypeptides and antibodies of	described below), boosting a T
			the invention (including	cell-mediated immune
			agonists or antagonists of the	response, and suppressing a T
			invention) to modulate IL-10	cell-mediated immune
			production and/or T-cell	response.
			proliferation include, for	
			example, assays such as	
			disclosed and/or cited in:	
			Robinson, DS, et al., "Th-2	
			cytokines in allergic disease"	
			Br Med Bull; 56 (4): 956-968	
			(2000), and Cohn, et al., "T-	
			helper type 2 cell-directed	
			therapy for asthma"	

	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method
Pharmacology & Therapeutics; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated	Caspase Apoptosis Rescue. Assays for caspase apoptosis rescue are well known in the art and may be used or routinely modified to assess the ability of the polypeptides of the invention (including
	Protection from Endothelial Cell Apoptosis.
	632
	HFTDZ36